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Supreme Court, U.S.
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No. _____

In the
Supreme Court of the United States

JOSEPH C. COLACICCO, INDIVIDUALLY
AND AS EXECUTOR OF THE ESTATE OF
LOIS ANN COLACICCO, DECEASED,
AND
BETH ANN MCNELLIS, ON BEHALF OF THE ESTATE OF
THEODORE DEANGELIS, DECEASED,
AND IN HER OWN RIGHT,
Petitioners,

v.

APOTEX, INC.; APOTEX CORP.,
A SUBSIDIARY OF APOTEX, INC.;
SMITHKLINE BEECHAM D/B/A GLAXOSMITHKLINE;
AND PFIZER, INC.
Respondents.

On Petition for a Writ of Certiorari
to the United States Court of Appeals
for the Third Circuit

PETITION FOR A WRIT OF CERTIORARI

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October 2, 2008

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QUESTION PRESENTED

Whether prior approval of a pharmaceutical label by the Food and Drug Administration ("FDA") preempts state-law failure-to-warn claims where FDA made no authoritative determination requiring or prohibiting a warning prior to the injury, but subsequently allowed warnings that parallel the state-law duty.

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PETITION FOR A WRIT OF CERTIORARI

Petitioners Joseph Colacicco and Beth Ann McNellis respectfully petition for a writ of certiorari to review the judgment of the court of appeals in this case.

INTRODUCTION

This case raises an issue of recurring importance in which the decision of the Third Circuit directly conflicts with that of the Vermont Supreme Court. This Court now has before it that conflicting case, *Wyeth v. Levine*. In this case, a divided panel erroneously held that the patients' claims for failure to provide adequate warnings were preempted by the Food and Drug Administration's approval of the label for the antidepressant drugs Paxil and Zoloft. Because the Court's resolution of *Wyeth v. Levine* is likely to provide needed guidance to the courts below on how to assess a preemption defense in this context, the petition should be held for the Court's disposition of *Wyeth v. Levine*, and then the case vacated and remanded for further proceedings in the Third Circuit.

Even independent of the Court's resolution of *Levine*, the petition here should be granted because this case raises important questions that are not likely to be resolved in *Levine*. In this case, unlike in *Levine*, FDA had given its attention to the issue involved in the patient's injury – the likelihood that antidepressants would paradoxically increase suicidal thoughts and behaviors, especially early in treatment -- before the patients were injured. Nonetheless, as of 2003 – when Lois Colacicco and Theodore DeAngelis committed suicide while taking Paxil and Zoloft, respectively – FDA had made no authoritative federal determination with respect to this risk, neither requiring nor

prohibiting a warning. The Third Circuit failed to recognize that this Court's opinion in *Sprietsma v. Mercury Marine*, 537 U.S. 51 (2002) controls the analysis and outcome of this case.

Furthermore, FDA was in the process of reanalyzing the risk of increased suicidality in 2003 when Paxil and Zoloft were prescribed to Ms. Colacicco and Mr. DeAngelis, and began to request warnings of this risk the following year. While FDA was engaged in its review, two antidepressant manufacturers exercised their power pursuant to 21 C.F.R. § 201.80(e) and § 314.70(c)(6)(iii)(A), adding warnings of increased suicidality without prior FDA approval. Both warnings were based on reanalyses of data that predated the prescriptions to Ms. Colacicco and Mr. DeAngelis. FDA did not claim that the added warnings were "false or misleading" and that the drugs were thus misbranded. Instead, FDA allowed the added warnings to stand for seven months in one instance and a full year in the other, until FDA began to require additional class-wide warnings for all antidepressants. Significantly, the second was an added warning issued by GlaxoSmithKline ("GSK"), the maker of Paxil, that Paxil posed more than six-fold increase in risk to adult patients – like Lois Colacicco – two and a half years after her death.

The Third Circuit below erroneously accepted the drug companies' arguments that both claims should be preempted by the 2003 labels, which FDA's subsequent regulatory actions and GSK's specific admission had demonstrated to be inadequate. The basis for the supposed conflict between state and federal law was that, if the drug companies had added a warning of

increased suicidality before FDA began to request it, the added warnings would have misbranded their drugs. That holding defies common sense and raises issues of surpassing importance that will not be addressed in *Wyeth v. Levine:* whether misbranding is a valid basis for conflict preemption when drug companies add warnings of the increased risk at issue without prior FDA approval and FDA does not pursue misbranding, and when FDA itself subsequently requests warnings of the increased risk -- but only after the patients' death or injury. Because federal regulation of prescription drugs expressly anticipates that risks will be reevaluated and warnings added as the drugs perform in the market, these issues arise with respect to many prescription drugs. Thus, this petition presents questions that are significant in their own right, and the Court should grant the petition irrespective of its handling of *Wyeth v. Levine.*

OPINIONS BELOW

The judgments of the court of appeals, in which *Colacicco v. Apotex, Inc., et al.* and *McNellis v. Pfizer, Inc.* were consolidated, are reprinted at App. 1-6. Its opinion is reported at 521 F.3d 253 (3d Cir. 2008) and is reprinted at App. 7-78.

The opinion and order of the district court in *Colacicco,* granting the defendants' motion to dismiss based on federal preemption, is reported at 432 F. Supp. 2d 514 (E.D. Pa. 2006) and reprinted at App. 79-162.

The original, unpublished opinion of the district court in *McNellis* denying summary judgment based on preemption is available at 2005 WL 3752269 and is

reprinted at App. 163-93. The subsequent order denying Pfizer's motion to vacate and certifying the summary judgment order for interlocutory appeal is reprinted at App. 194-96; and the court's unpublished opinion supporting that order is available at 2006 WL 2819046 and reprinted at App. 197-228.

JURISDICTION

The court of appeals entered its judgments on April 8, 2008, *see* App. 1-6, and denied Petitioners' timely petition for rehearing *en banc* on May 5, 2008, *see* App. 229-31. On July 24, 2008, Justice Souter extended the time for filing a petition for certiorari to and including October 2, 2008. This Court has jurisdiction under 28 U.S.C. § 1254(1).

CONSTITUTIONAL AND REGULATORY PROVISIONS INVOLVED

The Supremacy Clause of the United States Constitution is reprinted at App. 232. Section 201.80(e) of FDA's regulations, 21 C.F.R. § 201.80(e), which provides that a drug's label "shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved," is reprinted at App. 236-37. Section 314.70(c)(6)(iii)(A) of FDA's regulations, 21 C.F.R. § 314.70(c)(6)(iii)(A), which provides that a drug manufacturer may add or strengthen a warning without prior FDA approval, is reprinted at App. 238-41.

STATEMENT

A. Operative Facts. On October 6, 2003, Lois Colacicco's physician prescribed Paxil for her depression, and her prescription was filled with its generic equivalent. Three weeks later, at the age of 55, she killed herself. *See* App. 8-9.

On January 22, 2003, Theodore DeAngelis's physician prescribed Zoloft for his depression. He killed himself eight days later, at the age of 64. *See* App. 10.

B. The Evolution of Drug Labeling. FDA approves drugs based on a limited number of clinical trials, which are simply incapable of detecting many adverse reactions to the drug, or of providing adequate information about the drug's risks and benefits in a much broader population of people who are not typically as healthy or as carefully monitored as subjects in pre-marketing clinical trials.[1] Adverse reactions and side effects of approved drugs inevitably appear as the drug performs in the marketplace.[2] And this is where FDA is particularly lacking. FDA simply does not have

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[1] *E.g.*, FDA, *Clinical Therapeutics and the Recognition of Drug-Induced Disease* (June 1995) ("When a drug goes to market, we know everything about its safety . . . Wrong."), *available at* http://www.fda.gov/medwatch/articles/dig/ceart.pdf. "Clinical trials seldom detect, or define the frequency of, all important adverse effects." *Id.*

[2] According to a 1990 General Accounting Office report, for example, serious post-approval risks surfaced in more than one-half of the 198 drugs approved by FDA between 1976 and 1985, "as evidenced by labeling changes or withdrawal from the market." GAO, *FDA Drug Review, Post-Approval Risks 1976-85*, at 3 (1990), *available at* http://archive.gao.gov/d24t8/141456.pdf.

sufficient resources comprehensively to review and analyze all approved drugs in the post-marketing phase.[3] Thus, there is much information that is not submitted to FDA, both by statutory design and by omission.

The responsibility to review and analyze all safety information as a drug performs in the marketplace does not fall on FDA, but on drug manufacturers themselves. *See* 21 C.F.R. § 314.80(b). Because drug manufacturers will always have far superior knowledge of their drugs' safety issues, they must add warnings "as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." *Id.* § 201.80(e). Significantly, drug manufacturers have the power and the duty to add warnings without prior FDA approval. *See id.* § 314.70(c)(6)(iii)(A).

C. FDA Consideration of Antidepressants and Increased Suicidality. Prozac, the first of the modern antidepressants, was approved for treatment of depression in adults in 1987. The label submitted by Eli Lilly and approved by FDA mentioned suicide only as being inherent in depression. There was no indication that the drug could be a part of the problem rather than a part of the cure, or that taking an antidepressant might actually increase the risk of suicide early in treatment.

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[3] *See generally* David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims*, 96 GEO. L.J. 461, 486-91 (2008).

Following the publication of a study suggesting such an increased risk, however, two citizen petitions were filed with FDA in 1990 and 1991 seeking withdrawal of Prozac or a warning that Prozac caused increased suicidal thoughts and behaviors. In response, FDA convened an advisory committee, which concluded that it had insufficient data to require a warning that Prozac caused suicide. Nevertheless, FDA observed that "nobody in the agency dismisses the possibility that antidepressants in general or fluoxetine [Prozac] in particular may have – and I emphasize 'may' – the capacity to cause untoward injurious behaviors, acts, and/or intensify them."[4]

When FDA approved Paxil and Zoloft, their manufacturers proposed, and FDA approved, "inherent in [depression]" language similar to the Prozac label, and this language was still in place in 2003. App. 9-10. Until August 2003 (as discussed in section D below), no antidepressant manufacturer proposed the addition of any warning of an association between its drug and increased suicidality. Until 2004, FDA neither required nor prohibited a warning of this association to patients of any age.

In 2002, however, FDA's regulatory view began to change. On October 7, 2002, an FDA reviewer noted "numerous adverse events coded with terms such as hostility and emotional lability" in an application

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[4] PSYCHOPHARMACOLOGICAL DRUGS ADVISORY COMMITTEE, FDA (Rockville, Maryland) (Sept. 20, 1991)("1991 PDAC"), Hearing Tr. at 126. The full committee minutes are available at http://www.fda.gov/ohrms/dockets/ac/prozac/2443T1.PDF.

seeking approval of Paxil to treat pediatric patients.[5] On October 10, 2002, FDA requested that GSK "reanalyze its data and better characterize the adverse events identified under the term emotional lability."[6] When GSK submitted its response in May 2003, FDA learned that "almost all of these events [labeled 'emotional lability'] related to suicidality."[7] On June 3, 2003, FDA's Dr. Russell Katz wrote that GSK "has not proposed labeling changes, and makes a feeble attempt to dismiss the finding."[8] FDA then expanded the scope of its investigation and requested a reanalysis of pediatric data from other antidepressant manufacturers.[9]

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[5] Clinical Review of Pediatric Exclusivity Supplement for Paxil, FDA (Oct. 7, 2002) at 6, *available at* http://www.fda.gov/cder/foi/esum/2004/20031s037_paxil_Clincal_BPCA_FIN.pdf.

[6] *Amicus* Brief for the United States at 16-17, *Kallas v. Pfizer, Inc.*, Case No. 2:04CV0998 (D. Utah filed Sept. 15, 2005)("U.S. *Kallas Amicus* Br."), available at https://ecf.utd.uscourts.gov/doc1/1831186593.

[7] *FDA's Role in Protecting the Public Health: Examining FDA's Review of Safety and Efficacy Concerns in Anti-Depressant Use by Children: Hearings Before the Subcomm. on Oversight and Investigations of the H. Comm. on Energy and Commerce*, 108th Cong., 2nd Sess., Hearing Tr. at 135 (Sept. 23, 2004)("Sept. 23, 2004 Cong. Hearing Tr."), *available at* http://www.access.gpo.gov/congress/house/pdf/108hrg/96099.pdf.

[8] *Id.* at 136.

[9] U.S. *Kallas Amicus* Br. at 17.

FDA pooled the data it subsequently received from all antidepressant manufacturers and considered the effects of antidepressants as a class. When FDA's advisory committee convened to examine the reanalyzed pediatric data in February 2004, the chairman of the committee observed that "we do not believe that this data until now has been provided to us in a way that would permit us to interpret it fully."[10] After finally analyzing the pediatric data, FDA concluded that "[a] causal role for antidepressants in inducing suicidality has been established in pediatric patients" and began to require that warnings of increased suicidality be placed in a "black box."[11] A boxed warning is the strongest warning FDA regulations allow, short of contraindicating the use altogether. *See* 21 C.F.R. § 201.80(e), App. 237. FDA also requested that drug companies warn patients directly – rather than only through their physicians – via a Patient Medication Guide.[12] FDA subsequently requested that antidepressant manufacturers reanalyze their data concerning adult patients, as they had with the pediatric data.

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[10] PSYCHOPHARMACOLOGIC DRUGS ADVISORY COMMITTEE WITH THE PEDIATRIC SUBCOMMITTEE OF THE ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE, FDA (Bethesda, Maryland) (Feb. 2, 2004)("Feb. 2004 PDAC"), Hearing Tr. at 24. The full committee minutes are *available at* http://www.fda.gov/ohrms/dockets/ac/04/transcripts/4006T1.pdf.

[11] FDA, Labeling Change Request Letter for Antidepressant Medication (Oct. 15, 2004), *available at* http://www.fda.gov/cder/drug/antidepressants/SSRIlabelChange.htm.

[12] *Ibid.*

On March 22, 2004, while reanalysis of the pediatric data was still ongoing, FDA issued a public health advisory warning of the risk of increased suicidality to adult patients, "especially at the beginning of therapy."[13] In May 2004, GSK sent a "Dear Doctor" letter warning "both adult and pediatric" patients in conformance with the March 22, 2004 Public Health Advisory.[14] On June 30, 2005, FDA issued a second public heath advisory, warning that adults being treated with antidepressants, "particularly those being treated for depression," should be closely watched for increasing suicidal thoughts or behavior, especially "early in treatment."[15]

In 2007, FDA revised the class-wide portion of the label for all antidepressants, based on its reanalysis of the pooled adult data. Although the pooled data did not show a class-wide, increased risk in patients treated with antidepressants as compared to placebo beyond age 24, the black box (in the class-wide section of the label) was revised to warn that "[p]atients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for

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[13] FDA Public Health Advisory, *Worsening Depression and Suicidality in Patients Being Treated with Antidepressant [sic]* (Mar. 22, 2004), *available at* http://www.fda.gov/cder/drug/antidepressants/AntidepressanstPHA.htm.

[14] *See* "Dear Healthcare Professional" Letter from GSK (May 2004), *available at* http://www.fda.gov/medwatch/SAFETY/2004/Paxil_hcp.pdf.

[15] FDA Public Health Advisory, *Suicidality in Adults Being Treated with Antidepressant Medications* (June 30, 2005), *available at* http://www.fda.gov/cder/drug/advisory/SSRI200507.htm.

clinical worsening, suicidality, or unusual changes in behavior."[16]

D. The Two Warnings Added by Antidepressant Manufacturers Without Prior FDA Approval. On two occasions, antidepressant manufacturers have added warnings of increased suicidality associated with their drugs without prior FDA approval. On August 22, 2003, Wyeth sent out a "Dear Doctor" letter in which it warned of "increased reports among [pediatric patients] of hostility and suicide-related adverse events." The letter went on to state that Wyeth had "updated the prescribing information for Effexor" to warn of those increased reports of suicide risk.[17] FDA did not pursue misbranding against Wyeth for changing its label without prior approval. Instead, FDA emphasized that Wyeth's action was specifically permitted: "[i]t should be noted that sponsors have the authority to make changes of this nature, *i.e.*, that are perceived to strengthen labeling from the standpoint of safety, without prior approval by FDA."[18] FDA's Director of the

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[16] FDA, Revisions to Product Labeling (May 2, 2007), *available at* http://www.fda.gov/cder/drug/antidepressants/antidepressants_label_change_2007.pdf.

[17] "Dear Healthcare Professional" Letter from Wyeth (Aug. 22, 2003), *available at* http://www.antidepressantsfacts.com/2003-08-22-Wyeth-Effexor-kids.pdf.

[18] Memorandum, Background Comments for February 2, 2004 Meeting of PDAC and Peds AC, FDA, at 11 (Jan.5, 2005), *available at* http://www.fda.gov/ohrms/dockets/ac/04/briefing/4006B1_03_Background"%20Memo"%2001-05-04.pdf.

Office of Drug Evaluation confirmed in his testimony to Congress that FDA had allowed Wyeth's added precaution to stand, unaltered, for seven months, until it began to require even stronger class-wide warnings for all antidepressants in 2004.[19]

In May 2006, while the reanalysis of the adult data was ongoing, GSK issued its own warning pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A). Without prior FDA approval, it sent a "Dear Doctor" letter to alert physicians of its label change and to warn that "in the analysis of adults with [major depressive disorder](all ages), the frequency of suicidal behavior was higher in patients treated with [Paxil] compared with placebo," and that the difference was "statistically significant."[20] GSK's data demonstrated that patients taking Paxil were more than six times as likely to experience increased suicidal behavior as patients taking placebo and emphasized that "the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24."[21] This dramatic increase in risk was "not based

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[19] Sept. 23, 2004 Cong. Hearing Tr. at 85.

[20] "Dear Healthcare Professional" Letter from GSK (May 2006)("GSK May 2006 Warning"), *available at* http://www.fda.gov/MedWatch/safety/2006/paroxetineDHCPMay06.pdf.

[21] *Ibid.* *Compare* the actual wording of the added warning to the court of appeals' implication that it applied only to "young adults." App. 49 n.18.

on new data," but on a reanalysis of old data.[22] Again, FDA did not pursue a misbranding action (or any other type of enforcement proceeding) against the manufacturer. GSK's added warning stood unchanged for a full year, until FDA again requested that all antidepressant labeling be revised to contain certain warnings in a class-wide portion of the drug's label, uniform for all antidepressants.

Other than these two instances, no antidepressant manufacturer has ever proposed or added a warning of increased suicidality until FDA has requested it to do so. FDA has never rejected any strengthened warning of increased suicidality proposed by any antidepressant manufacturer.

E. Proceedings Below.

1. The defendants in *Colacicco* moved to dismiss the claims against them pursuant to Federal Rule of Civil Procedure 12(b)(6), based on federal preemption. They claimed that if they had added a warning of increased suicidality before FDA requested it, the added warning would have misbranded the drug. On May 25, 2006, the district court granted that motion. *See* App. 162. Significantly, the district court noted that "it is not in dispute that the FDA's position is a hypothetical," App. 104, but believed it was required to give conclusive deference to FDA's new litigation position that the claims were preempted rather than follow the many "forceful" opinions failing

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[22] Report of Joseph Glenmullen, M.D. at 58 (Aug. 10, 2007)("Glenmullen Report"), *available at* http://finance.senate.gov/press/Gpress/2008/prg061208a.pdf.

to find preemption of antidepressant cases, App. 120. The court "concluded not that [the] analysis [in those opinions] is wrong, but that it is improper for a federal district judge to engage in this analysis in the first place." App. 120.

2. Pfizer, the defendant in *McNellis*, moved for summary judgment, likewise claiming preemption based on misbranding. On December 29, 2005, the court denied Pfizer's motion. *See* App. 193. The district court based its decision on its finding that FDA regulations expressly envisioned that the approved labeling would evolve as the drug performed in the marketplace. *See* App. 172, 175-76.

Pfizer moved the court to vacate its decision in light of subsequent statements by FDA and the district court decision in *Colacicco*. On September 29, 2006, the district court denied the motion to vacate, disagreeing with the deference the district court in *Colacicco* had given to FDA's position, *see* App. 194-96, 221, and commenting that "the abrupt rejection of the agency's own prior interpretation (while the regulations themselves are unchanged) suggests a degree of informality yielding an interpretation unhinged from the text and original intent of the regulations themselves," App. 218. The court did certify for interlocutory appeal the following question: "Whether that the United States Food and Drug Administration's requirements for the form and content of the labeling for the prescription antidepressant Zoloft preempted New Jersey's failure-to-warn law, under the doctrine of conflict preemption, where the FDA's regulations at 21 C.F.R. 201.57(e) and 314.70(c)(6)(iii) permit a manufacturer to unilaterally enhance its warning when

the manufacturer has reasonable evidence of an association of a serious hazard with a drug." App. 196.

3. The Third Circuit consolidated the two cases on appeal. On April 8, 2008, in a divided opinion, the court of appeals wrote that "[t]he scarcity of actual conflict cases has led the Justices to pose hypothetical conflicts" as the basis for conflict preemption. App. 32. The court viewed it as immaterial that FDA had never actually rejected a warning of increased suicidality added by an antidepressant manufacturer, App. 47, but focused on FDA's failure to require a warning as of 2003. The court wrongfully equated FDA's failure to require a warning with a prohibition of the warning, finding preemption in "circumstances in which the FDA has publicly rejected the need for a warning that plaintiffs argue state law requires," App. 46. The majority affirmed *Colacicco* and reversed *McNellis*.

Judge Ambro dissented, emphasizing FDA's "180-degree reversal" of its historical position on preemption, App. 65 (citation omitted), and observing that "[n]one of the drug manufacturers in these cases attempted to enhance a warning and received an FDA sanction in response," App. 70. Because "[d]rug manufacturers have the best information about the safety of their products," he found it logical that they had the power under the regulations to add warnings without prior FDA approval, App. 71. Judge Ambro was unwilling to find preemption under these circumstances.

4. Petitioners sought rehearing *en banc*, which was denied. *See* App. 229-31.

REASONS FOR GRANTING THE PETITION

I. THE COURT SHOULD HOLD THIS PETITION PENDING ITS OPINION IN *WYETH V. LEVINE.*

Because the Court's resolution of *Levine* likely will provide needed guidance to the courts below, the Court should hold this petition and then vacate and remand for further proceedings in light of *Levine*.

A. There Are Express Conflicts Between the Court of Appeals' Opinion in This Case and the Vermont Supreme Court's Opinion in *Levine*. The court of appeals' decision in this case directly conflicts with the Vermont Supreme Court's decision in several respects.

1. Hypothetical Conflicts. The asserted basis for conflict preemption in this case is that if the drug manufacturers had added a warning of increased suicidality in 2003, before FDA requested such warnings, they would have misbranded their drugs.[23] Because no antidepressant manufacturer actually proposed or added any such warning with respect to adult patients prior to the prescriptions to Ms. Colacicco and Mr. DeAngelis, however, "it is not in dispute that the FDA's position is a hypothetical," App. 104. This Court has instructed that "[t]he existence of a

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[23] Conflict preemption based on hypothetical misbranding is before this Court in *Levine*. *See* Brief for the United States as *Amicus Curiae* Supporting Petitioner at 21, *Wyeth v. Levine*, No. 06-1249 (U.S. filed June 2, 2008)("U.S. *Levine Amicus* Br."); Brief for Respondent Diana Levine at 34, *Wyeth v. Levine*, No. 06-1249 (U.S. filed August 7, 2008)("Resp. *Levine* Br.").

hypothetical or potential conflict is insufficient to warrant the preemption of" state law. *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982).

The Vermont Supreme Court correctly rejected hypothetical misbranding as a basis for conflict preemption. 944 A.2d at 189 n.3. In contrast, the Third Circuit held that a hypothetical conflict can form the basis for conflict preemption, noting that "[t]he scarcity of actual conflict cases has led the Justices to pose hypothetical conflicts." App. 32. With due respect to the court of appeals, it has misunderstood the opinions of this Court. It is true that this Court has sometimes posed hypotheticals in its analysis of conflict issues. It is not true that the Court has held that a hypothetical conflict can form the basis for conflict preemption. *See, e.g., Rice,* 458 U.S. at 664 (Hypothesizing scenarios that might result in a conflict "ignore[s] the teaching of this Court's decisions which enjoin seeking out conflicts between state and federal regulation when none clearly exists."). Such a holding would be particularly inappropriate in the prescription drug context, where Congress has disclaimed preemption absent a "direct and positive conflict" with state law. Drug Amendments of 1962, Pub. L. No. 87-781 § 202, 76 Stat. 793, App. 232.

The court of appeals used the example of this Court's opinion in *Florida Lime & Avocado Growers, Inc. V. Paul*, 373 U.S. 132, 142-43 (1963), writing that "the Supreme Court hypothesized the existence of an impossibility conflict." App. 32. What the Court actually observed in *Paul* is that there might be an impossibility conflict if the state and federal statutes were written so that it was impossible to comply with

both. But they were not. "No such impossibility of dual compliance is presented on this record, however." *Paul*, 373 U.S. at 143.[24]

If any antidepressant manufacturer had attempted to give an appropriate warning prior to January or October 2003, FDA could have evaluated the added warning. If FDA had considered the added warning to be "false or misleading," it could have pursued a case for misbranding in federal court. *See* 21 U.S.C. § 321(n), §§ 331(a-b), 332, 333, 352(a). Unless FDA actually takes appropriate legal action, however, "misbranding" remains a speculative concept.[25]

2. The Federal Regulation Allowing a Drug Manufacturer To Add or Strengthen a Warning Without Prior FDA Approval. The court of appeals in this case acknowledged that drug manufacturers have the power to add a warning without prior FDA approval pursuant to § 314.70(c)(6)(iii)(A), but found conflict preemption in the face of this acknowledged power. App. 38, 56. The

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[24] In the other example cited by the Third Circuit, the Court found that there was an "irreconcilable conflict" between state and federal statutes where "the Federal Statute authorizes national banks to engage in activities that the State Statute expressly forbids." *Barnett Bank of Marion County, N.A. v. Nelson*, 517 U.S. 25, 31 (1996). The conflict that the Court found was not hypothetical, but an actual conflict grounded in the language of the statutes.

[25] The government inadvertently emphasized the extreme unlikelihood of misbranding at oral argument, when FDA's counsel admitted that she knew of no instances in which FDA had claimed misbranding as a result of a drug manufacturer's strengthening a warning. App. 71.

court of appeals attempted to distinguish *Levine*, claiming that the evidence in this case showed FDA's intention to prohibit a warning of increased suicidality. App. 46 n.17. As Petitioners discuss *infra*, the court of appeals wrongfully equated FDA's failure to require a warning with a prohibition of the warning.

In contrast, the Vermont Supreme Court cited a drug manufacturer's power to add a warning without prior FDA approval under 21 C.F.R. § 314.70(c)(6)(iii)(A) to demonstrate that it is not impossible to comply with federal labeling requirements and concurrently to give an adequate warning under state law. 944 A.2d at 188-89. The dissenting judge in the court of appeals understood this regulation in the same manner: "to avoid discouraging the party with the best safety information from coming forward, 21 C.F.R. § 314.70 permits a manufacturer to alter a drug label before the FDA has evaluated and approved the change." App. 71. Both parties in Levine have briefed this issue,[26] and the Court's interpretation of the regulation in *Levine* will impact the resolution of these cases.

3. Deference to FDA's Changed Position Regarding Preemption. The dissenting judge in the court of appeals reviewed FDA's historical position on preemption, concluding that "FDA has for over three-quarters of a century viewed state tort law as complementary to its warning regulations. Only for the last two years has it claimed otherwise." App. 78. He

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[26] *See* Brief for Petitioner Wyeth at 10, 34-40, *Wyeth v. Levine*, No. 06-1249 (U.S. filed May 27, 2008)("Pet. *Levine* Br."); Resp. *Levine* Br., at 7, 37-38.

ultimately concluded that FDA's new position on preemption deserves little deference. App. 66. The Vermont Supreme Court was more blunt, according FDA's position "no deference." 944 A.2d at 193. Although the majority of the court of appeals was unwilling to defer its entire preemption analysis to FDA as the district court in *Colacicco* had done, App. 120, the majority found that "FDA's view is entitled to some degree of deference," App. 55. *Levine* also involves the level of deference to be accorded to FDA's litigation position,[27] and the Court's opinion will be instructive in these cases.

B. The Parties in *Levine* Have Raised Other Issues That Will Provide Guidance in These Cases. In addition to the express conflicts between the court of appeals' decision and *Levine*, there are other issues before the Court in *Levine* that could affect – and might well be dispositive of – this case. One such issue is whether misbranding under the federal statutes parallels failure to warn claims under state law, which has been raised and briefed in *Levine*.[28] Federal law does not preempt state actions that parallel federal law. *Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1011 (2008); *Bates v. Dow AgroSciences LLC*, 544 U.S. 431, 447-49 (2005). A drug is misbranded if it "fails to reveal facts . . . material with respect to consequences which may result from the use of the article," 21 U.S.C. § 321(n). *Cf. Bates*, 544 U.S. at 438. When Paxil was prescribed to Lois Colacicco in October 2003, there was no warning

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[27] *See* Pet. *Levine* Br. at 39, 43; Resp. *Levine* Br. at 39, 55-56.

[28] *See* Resp. *Levine* Br. at 26-27, 33, 45, 50.

that the drug itself was associated with increased suicidality. Two and a half years later, GSK issued its Dear Doctor letter, warning of a more than six-fold increase in suicidal thoughts and behaviors in adult patients treated with Paxil as compared to those treated with placebo.[29] GSK's added warning demonstrated that Paxil was misbranded by omission when it was prescribed to Lois Colacicco because the 2003 label for Paxil failed to adequately warn of its risks. As such, Petitioners' failure-to-warn claims do not conflict with federal misbranding standards at all. They parallel them. The likely effect of the Court's holding in *Levine* on this issue is yet another reason to hold this petition, and then to grant, vacate and remand for further proceedings in light of *Levine*.

II. NO MATTER HOW THE COURT DECIDES *LEVINE*, THIS CASE PROVIDES AN IDEAL VEHICLE TO FURTHER DEFINE IMPORTANT CONTOURS OF PREEMPTION ANALYSIS IN PRESCRIPTION DRUG CASES.

There are several issues of substantial importance in these cases which are not involved, or only tangentially involved, in *Levine*. In general, these issues arise from the nature of federal regulation of prescription drugs. The federal regulations expressly anticipate that risks will be reevaluated and warnings added as the drugs perform in the market. *See* 21 C.F.R. § 201.80(e) and § 314.70(c)(6)(iii)(A). Because the nature of the system is that warnings will be periodically added or strengthened, prescription drug

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[29] GSK May 2006 Warning.

labels necessarily evolve over time. Given that evolution, there are significant difficulties with attempts to "freeze" an ongoing process and to determine whether the FDA-approved label at a particular point in time should be preemptive.

As this Court has observed with respect to industries in which warning labels "evolve over time," "tort suits can serve as a catalyst" in the evolution. *Bates*, 544 U.S. at 449. This also underscores the wisdom of Congress in foreclosing preemption absent a "direct and positive conflict" with state law. 1962 Amendments § 202, 76 Stat. 793, App. 232. The issues identified below are important to many prescription drug cases, and this case presents an ideal vehicle for their consideration, irrespective of the decision in *Levine*.

A. The Court of Appeals Failed To Recognize That *Sprietsma* Controls the Disposition of This Case. This Court's decision in *Sprietsma* squarely addresses the situation regarding antidepressants and increased suicidality prior to 2004.[30] In *Sprietsma*, the Court acknowledged that "a federal decision to forgo regulation in a given area may imply an authoritative federal determination that the area is best left *un*regulated, and in that event would have as much pre-emptive force as a decision *to* regulate." *Id.* at 66 (citation and internal quotations

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[30] *Sprietsma* was briefed in *Levine* as well, *see* Resp. *Levine* Br. at 53. In *Levine*, however, there is no evidence that FDA ever focused its attention on the administration of Phenergan by IV-push, whereas these cases present a scenario in which *Sprietsma* is more directly applicable.

omitted, italics in original). But the Court will not imply an authoritative federal determination against regulation simply because an agency has given some attention to a particular subject. Even where the agency "carefully consider[s]" an issue and consciously refuses to require action under federal law, its decision is not preemptive unless the decision rises to the level of an authoritative federal determination that prohibits action on the state level. *Id.* at 67.

As the government explained in its *amicus* brief in *Sprietsma*, "[e]ven where a federal agency has focused its attention on a particular subject matter within its jurisdiction, it may have various reasons for concluding that federal regulation is inappropriate. The agency may believe that the available evidence is too inconclusive to warrant the imposition of a prescriptive standard under the criteria set forth in the relevant federal statute."[31] FDA's failure to require a warning of increased suicidality associated with antidepressants prior to 2004 reflected only that FDA had not required a warning based on the evidence then before it – not an authoritative federal determination prohibiting one.

While FDA found that the Prozac data it examined in 1991 were not sufficient to require a warning of increased suicidality,[32] FDA's official spokesman confirmed that there was no authoritative

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[31] Brief for the United States as *Amicus Curiae* Supporting Petitioner at *17, *Sprietsma v. Mercury Marine*, 537 U.S. 51 (2002)(No. 01-706), 2002 WL 500643 ("U.S. *Sprietsma Amicus* Br.").

[32] The court of appeals discussed the 1991 PDAC, but overstated its conclusion. *See* App. 41.

determination prohibiting such a warning: "[N]obody in the agency dismisses the possibility that antidepressants in general or fluoxetine [Prozac] in particular may have – and I emphasize 'may' – the capacity to cause untoward injurious behaviors, acts, and/or intensify them."[33]

Furthermore, in response to the 1991 citizen petition, FDA wrote that "an actual court finding of a causal relationship" would be significant.[34] "In that event, the agency would be able to evaluate the scientific basis for the court's conclusion, and consider whether the court's conclusion warranted a modification of its own position."[35] If FDA had considered its action in refusing to require a warning to be an "authoritative federal determination" prohibiting a manufacturer's addition of such a warning pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A), court cases would of course be preempted and there could not be an "actual court finding."

FDA's response to the Prozac petitions is analogous to the Coast Guard's decision not to require propeller guards in its 1990 letter, which the Court discussed in *Sprietsma*. Although the Coast Guard did not require guards, it emphasized that it would

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[33] 1991 PDAC at 126.

[34] Letter from Carl C. Peck, M.D. to Sanford Block, Executive Director of Citizens Commission on Human Rights (July 26, 1991), *available at* https://ecf.wyd.uscourts.gov/doc1/2071540001. An "actual court finding" would come 10 years later, *infra* at 30.

[35] *Id.*

"continue to collect and analyze accident data for changes and trends."[36] "The letter thus expressly contemplated continuing federal scrutiny of the propeller guard issue in light of additional information, including information regarding the development of new safety devices."[37] Just as the Coast Guard continued to consider safety data concerning propeller guards after its 1990 letter, FDA continued to consider the relationship between increased suicidality and antidepressants after its denial of the citizen petitions in 1992, and even requested further studies to investigate the phenomenon.[38]

GSK, Pfizer, and other antidepressant manufacturers sought and received FDA approval of various indications over the ensuing years, and FDA denied another citizen petition regarding Prozac in 1997. But until Wyeth issued its Dear Doctor letter in August 2003, no antidepressant manufacturer ever proposed adding, or actually added pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A), a warning of an association between its drug and increased suicidality. FDA thus never rejected any such warning.

Nonetheless, the court of appeals repeatedly wrote that FDA "rejected" such a warning. *E.g.*, App. 40, 45. While the court acknowledged that "a court could more easily determine the preemption issue if the FDA had formally rejected such a CBE supplement,"

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[36] U.S. *Sprietsma Amicus* Br. at *27-28.

[37] *Id.* at *28.

[38] 1991 PDAC at 128. No further studies were ever done.

App. 47, it wrongly equated FDA's refusal to require a warning with a rejection of any such warning. This appears clearly when the court purports to limit its holding to "circumstances in which the FDA has publicly rejected **the need** for a warning. *Id.* at 33 (boldface added). FDA's rejection of the need for a warning is merely a failure to require the warning.

The court of appeals repeated the mistake made by the Illinois Supreme Court, which had concluded "that the Coast Guard's failure to promulgate a propeller guard requirement here equates to a ruling that no such regulation is appropriate pursuant to the policy of the FBSA." *See Sprietsma*, 537 U.S. at 66 (citation omitted). The Illinois Supreme Court overstated the impact of that failure to require. The Coast Guard had simply concluded, "given the evidence available *at that time*, that affirmative imposition of a federal propeller guard requirement could not be justified under the relevant statutory criteria."[39] Just as the Illinois Supreme Court improperly gave preemptive weight to the Coast Guard's decision not to require propeller guards, the court of appeals did the same regarding FDA's pre-2004 decision not to require warnings of increased suicidality. *Sprietsma*, 537 U.S. at 65 ("It is quite wrong to view that decision as the functional equivalent of a regulation prohibiting all States and their political subdivisions from adopting such a regulation."). Likewise, both courts misread this Court's holding in *Geier v. American Honda Motor Co.*, 529 U.S. 861 (2000), which "does not suggest that common-law suits will be preempted whenever the federal agency has focused its attention upon the

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[39] U.S. *Sprietsma Amicus* Br. at *27 (italics in original).

particular aspect of motor vehicle (or recreational vessel) performance that forms the basis of the plaintiff's claim."[40]

When FDA's advisory committee convened to examine the reanalyzed pediatric data in February 2004, however, it erased any doubt that there had been any prior "authoritative federal determination" on the antidepressant/suicide issue. The chairman observed that "we do not believe that this data until now has been provided to us in a way that would permit us to interpret it fully."[41] In his testimony to Congress later that year, FDA's Director of the Office of Drug Evaluation explained why the FDA had not seen the increased signal earlier: "what we conceivably could have asked but didn't know to ask was a better, more structured, more careful look at events that might or might not represented [sic] suicidality, but we didn't know to do that."[42] FDA did not even request drug manufacturers to reanalyze their data concerning adult patients until after it completed its review of the pediatric data in 2004. Under the holding in *Sprietsma*, therefore, FDA had made no authoritative

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[40] U.S. *Sprietsma Amicus* Br. at *19. In its *amicus* brief in *Levine*, the government opined that, as long as FDA "considered" data concerning a potential side effect of a drug but did not require a warning, that failure to require preempts a state-law claim predicating liability on the failure to warn of that side effect. U.S. *Levine Amicus* Br. at 25. Based on its *amicus* brief in *Sprietsma*, the government would have taken the opposite view six months earlier.

[41] Feb. 2004 PDAC at 24.

[42] Sept. 23, 2004 Cong. Hearing Tr. at 113.

determination that could form the basis of conflict preemption at the time of either death involved in this case.

B. When Conflict Preemption Is Based on Misbranding, FDA's Reaction to Warnings That Were Actually Added Is More Persuasive Than Its Hypothetical Reaction to Warnings That Were Not. Although conflict preemption based on hypothetical misbranding is before the Court in *Levine*, the case at bar presents important questions in the analysis that are not involved in *Levine*. Even if the Court allows hypothetical misbranding as a basis for conflict preemption in some instances, the Court should grant certiorari in this case to address how these issues affect the analysis.

Specifically, there are two actual instances in which antidepressant manufacturers added warnings of an association with increased suicidality, without prior FDA approval. In each instance, the manufacturer based the added warning on a reanalysis of long-existing data. In neither instance did FDA pursue misbranding. Petitioners assert that FDA's actual reaction to warnings that were added is far more persuasive than its hypothetical reaction to warnings that were not.

Wyeth added its precaution to pediatric patients on August 22, 2003, six weeks before Paxil was prescribed to Lois Colacicco. It is true that Wyeth's added warning addressed pediatric patients, not adult patients such as Mr. DeAngelis or Ms. Colacicco. But as of 2003, FDA's position regarding adult and pediatric patients was the same: it had neither required nor

prohibited a warning of increased suicidality. Furthermore, FDA would later claim in an *amicus* brief filed on September 15, 2005 that such a warning added in October-November 2002 would have misbranded Zoloft with respect to a pediatric patient.[43] FDA apparently takes the position that an added warning before it required it would have misbranded an antidepressant as to any patient, pediatric or adult.

Of even more significance is the warning added by GSK in May 2006 with respect to the use of Paxil by adult patients. FDA allowed this added warning to stand unchallenged for a full year, and admitted in its *amicus* brief in the court of appeals that it "did not reject the proposed labeling change."[44] FDA as regulator had evaluated a warning added without its prior approval, concerning the same drug, the same side effect and the same patient group, and had not claimed misbranding. FDA as litigator claimed that FDA would have reacted differently to the same warning, with the same scientific support from the manufacturer, three years earlier.[45]

Furthermore, it is important to note that allegations of misbranding are almost always decided by juries. *See* 21 U.S.C. §§ 332, 334(b), 337(a); *cf. Bates*, 544 U.S. at 452. Only one jury has passed on the relationship between Paxil and suicide, and it did so two years **before** the prescriptions to Mr. DeAngelis and Ms. Colacicco. On June 6, 2001, a unanimous

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[43] *See* U.S. *Kallas Amicus* Br. at 38.

[44] U.S. 3d Cir. *Amicus* Brief at 14.

[45] *Id.* at 16, 19.

federal jury in Wyoming found that Paxil "can cause some individuals to commit homicide and/or suicide." *Tobin v. SmithKline Beecham Pharms.*, 164 F. Supp. 2d 1278, 1287-88 (D. Wyo. 2001). The district court found the plaintiffs' evidence "scientifically reliable" and "legally admissible" under *Daubert v. Merrill Dow Pharms,,* 509 U.S. 579 (1993), both before trial and after. 164 F. Supp. 2d at 1283.

The court of appeals cited GSK's added warning in a footnote and mistakenly believed that it applied only to "young adults." App. 49 n.18. The majority opinion did not mention Wyeth's added warning, although the dissenting justice did so. *See* App. 71. Neither opinion cited *Tobin.* If hypothetical misbranding can establish a "direct and positive conflict" in some instances, the Court should clarify that the analysis of that conflict should place significant weight on warnings that were actually added, FDA's reaction to those warnings and actual jury verdicts concerning the warnings.

C. The Court Should Clarify Whether It Is Appropriate To Consider Subsequent Regulatory Events in an Analysis of Conflict Preemption by Misbranding. Courts have struggled to determine whether to "freeze" the misbranding analysis or whether and to what extent they should consider subsequent regulatory events. Misbranding is an allegation that must be proven in court, and there is no misbranding without a judgment. To claim misbranding as the basis for conflict preemption without a trial, however, FDA has attempted to vest itself with more power than it actually has. That is why, in its initial *amicus* brief making this assertion,

FDA characterized misbranding as a "self-executing statutory prohibition."[46] If misbranding were "self executing," analysis of a potential conflict at a certain point in time might be appropriate without a misbranding action. But it is not.

Most courts analyzing the issue have concluded that the subsequent warnings were relevant, at least to some extent.[47] The district court in *McNellis* agreed, concluding that "[i]n recommending label changes that reflect concerns about the association between SSRIs and suicidality, neither the FDA nor Pfizer can now claim, as they had in *Motus,* that no scientific basis exists for a suicide warning." App. 185. But FDA has remained undeterred, to the point that its litigation positions have become untethered to its regulatory activities.

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[46] Brief for the United States as *Amicus Curiae* in Support of the Defendant-Appellee at 19, *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004)(Nos. 02-55372, 02-55498), 2002 WL 32303084.

[47] *E.g., Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 730 (D. Minn. 2005)("[T]he FDA has since distanced itself from the substance of the *Motus* brief by recommending labeling changes that, in fact, reflect concerns about the association between SSRIs and suicidality. Thus, the Court has 'reason to suspect that the [*Motus* brief's] interpretation does not reflect the agency's fair and considered judgment on the matter in question.'"(*quoting Auer v. Robbins*, 519 U.S. 452, 462(1997))); *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 885-86 (E.D. Tex. 2005)("Given the hearings by both Congress and the FDA regarding suicidality, the FDA's PDAC's recent decision to recommend black box warnings regarding suicidality in children and adolescents, and the numerous experts who have concluded that there is a link between SSRIs, like Zoloft, and suicidality, it would be **inconceivable** to this Court to argue that an additional warning regarding suicidality would be false or misleading.")(boldface added).

FDA's *amicus* brief in *Kallas v. Pfizer* provides a clear example. Shyra Kallas was a pediatric patient whose physician prescribed Zoloft on October 8, 2002. She shot herself on November 4, 2002. At the time of her prescription and death, FDA had not yet required the black box warnings to pediatric patients (although it had already seen a signal and had asked GSK to reanalyze its data). By the time the government filed its *amicus* brief on September 15, 2005, however, it had been almost a full year since FDA had requested that a warning of the same side effect that led Shyra Kallas to take her own life be placed in a black box. Nonetheless, FDA claimed preemption because "Shyra Kallas' death preceded FDA's receipt of the May 2003 Paxil report, FDA's request for and receipt of additional information from antidepressant New Drug Application sponsors, Columbia University's reclassification of the sponsors' data, and FDA's preliminary and subsequent analysis of the sponsors' data. Thus, in October/November 2002, FDA did not believe that there was reasonable evidence of an association between Zoloft and an increased risk of suicidality in either adult or pediatric patients."[48] FDA wrongly attempted to equate its own "judgment"to a "self-executing statutory prohibition."[49]

The Third Circuit appeared at first to freeze the analysis in this case: "Our focus is on the period before the two deaths that are the subject of the actions before us." App. 48. The court then proceeded to discuss some of the regulatory events that came in the following years, *see* App. 48-51, ostensibly using the subsequent

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[48] U.S. *Kallas Amicus* Br. at 36.

[49] *E.g.*, U.S. *Kallas Amicus* Br. at 26, 34, 38.

events to bolster misbranding in 2003, *see* App. 50. If subsequent events were not relevant, *Sprietsma* is dispositive. If subsequent events were relevant, surely GSK's admission of a more than six-fold elevation of risk in May 2006 is conclusive evidence against misbranding. The conclusion should be the same in this particular case, but the analysis is very different.

Because risks are always being evaluated and warnings are periodically added to drug labels, the point in time at which to analyze conflict preemption based on misbranding becomes critical. If the Court allows hypothetical misbranding to serve as a basis for conflict preemption, it should clarify the extent to which subsequent regulatory events are relevant to the analysis.

D. *Buckman* Does Not Preclude Consideration or Evidence That a Drug Manufacturer Withheld or Manipulated Data in a Failure-to-Warn Case. The court of appeals refused to consider evidence that GSK had manipulated data it had submitted to FDA concerning Paxil, citing this Court's opinion in *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341 (2001). *See* App. 48. This interpretation, which allows a drug company to exclude evidence that it has withheld or manipulated data submitted to FDA and to then successfully claim conflict preemption because the agency has not required a warning, is an incorrect reading of *Buckman*. Although the Third Circuit is not alone in using

Buckman in this manner,[50] its interpretation is no less mistaken.

This Court held in *Buckman* that a claim of fraud on FDA is solely FDA's to pursue and is thus preempted by federal law. The Court differentiated a claim of fraud on FDA from a claim based on "traditional state tort law principles of the duty of care," 531 U.S. at 352, and emphasized in particular that reliance by FDA, absent acts affirmatively showing reliance, is peculiarly within FDA's knowledge, *id.* at 353 (Stevens, J., concurring). The government, appearing as *amicus curiae*, acknowledged the narrowness of the issue: "The fraud claim is preempted, but if there is negligent design, negligent manufacturing, failure to warn, common law malpractice, all of those claims are available." Transcript of Oral Argument at 19, *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001)(No. 98-1768).

This case illustrates the absurdity of reading *Buckman* as an evidentiary exclusion case. On June 12, 2008, Sen. Grassley (R-Iowa), the ranking member of the Senate Committee on Finance, formally asked FDA to investigate whether GSK had withheld safety information regarding the use of Paxil by adults. In his floor statement, Sen. Grassley alluded to drug

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[50] Two district courts have also held that *Buckman* precluded consideration of the manipulation of the Paxil data, *see Mason v. SmithKline Beecham Corp.*, 546 F. Supp. 2d 618, 627 n.5 (C.D. Ill 2008); *O'Neal v. SmithKline Beecham Corp.*, 551 F. Supp. 2d 993, 997 n.8 (E.D. Cal. 2008), while one has reached an opposite conclusion, squarely refusing to read *Buckman* as an evidentiary exclusion case, *see Knipe v. SmithKline Beecham Corp.*, No. 06-3024, 2008 WL 4090995 at *23 n.31 (E.D. Pa. Aug. 28, 2008).

companies' "hiding data," then clarified that "I don't mean that they actually hide the data. But they make these numbers so difficult to find that they might as well be invisible."[51] He concluded that, "[e]ssentially, it looks like GlaxoSmithKline bamboozled the FDA."[52]

Sen. Grassley's allegations are based on GSK's improper reporting of suicidal events in adult patients in its initial NDA for Paxil and in follow-up reports to the FDA between 1989 and 1992. The true data "demonstrate[] a causal link between the antidepressant and suicidal behavior. This has been true since 1989 although the 'bad' Paxil numbers obscured the risk for a decade-and-a-half."[53] GSK's manipulation of the data hid the fact that adult patients treated with Paxil are many times as likely to experience increased suicidal thoughts and behavior than patients treated with placebo, until it finally admitted to a more than six-fold increase in the risk in its May 2006 "Dear Doctor"letter – 17 years later.[54] "GlaxoSmithKline's failure to provide the correct data to the FDA in 1991 when the FDA was trying to get to the bottom of this potentially lethal side effect delayed

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[51] Floor Statement of Sen. Chuck Grassley, *Hidden Data on Paxil* (June 11, 2008), *available at* http://finance.senate.gov/press/Gpress/2008/prg061208.pdf.

[52] *Id.*

[53] Glenmullen Report at 74.

[54] GSK May 2006 Warning.

warnings for 15 years and placed countless people at risk."[55]

When the asserted conflict is that an added warning would have been "false or misleading," evidence that demonstrates that the drug manufacturer manipulated data that it submitted to FDA, and that the actual data demonstrate[] that the warning is neither false nor misleading, should be relevant. This reasoning is analogous to the Second Circuit's in *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85 (2d Cir. 2006), *aff'd sub nom. by an equally divided court, Warner-Lambert Co. v. Kent*, 128 S. Ct. 1168 (2008). The Sixth Circuit disagreed with the Second Circuit in *Garcia v. Wyeth-Ayerst Labs*, 385 F.3d 961, 966 (6th Cir. 2004), resulting in the conflict that was presented in *Kent*. The Court should grant this petition to clarify that *Buckman* does not allow exclusion of evidence that a drug company withheld or manipulated data, and that consumers in a failure-to-warn case may use such evidence to defeat preemption in a traditional failure to warn case.

CONCLUSION

The petition for writ of certiorari should be held pending the Court's decision in *Wyeth v. Levine*, after which the Court should grant the petition, vacate the judgment below, and remand for reconsideration in light of *Levine*. In the alternative, the Court should grant the petition and schedule the case for briefing and hearing on the merits.

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[55] Glenmullen Report at 14.

Respectfully submitted,

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APPENDIX

UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

No. 06-3107

JOSEPH C. COLACICCO,
INDIVIDUALLY AND AS EXECUTOR OF THE ESTATE
OF LOIS ANN COLACICCO, DECEASED,
Appellant

v.

APOTEX, INC.; APOTEX CORP., A SUBSIDIARY OF
APOTEX, INC.; SMITHKLINE BEECHAM,
d/b/a GLAXO SMITHKLINE

On Appeal from the United States District Court
for the Eastern District of Pennsylvania
(D.C. No. 05-cv-05500)
District Judge: Honorable Michael M. Baylson

Before: SLOVITER, AMBRO, Circuit Judges, and
RESTANI*, Judge

JUDGMENT

This case came on to be heard on the record from the United States District court for the Eastern District of Pennsylvania and was argued on December 10, 2007.

On consideration whereof, it is now hereby ADJUDGED and ORDERED that the judgment of the District Court entered May 26, 2006, be and the same is hereby affirmed.

Costs taxed against the Appellant. All of the above in accordance with the opinion of this Court.

Attest:

/s/ Marcia M. Waldron
Clerk

DATED: April 8, 2008

*Hon. Jane A. Restani, Chief Judge, United States Court of International Trade, sitting by designation.

UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

No. 06-5148

BETH ANN MCNELLIS,
ON BEHALF OF THE ESTATE OF THEODORE DEANGELIS,

DECEASED AND IN HER OWN RIGHT

v.

PFIZER INC.; JOHN DOES 1-5; ABC DOE CORP.; DEF DOE CORP., GHI DOE CORP.

PFIZER INC.,
Appellant

On Appeal from the United States District Court
for the District of New Jersey
(D.C. No. 05-cv-01286)
District Judge: Honorable Jerome B. Simandle

Before: SLOVITER, AMBRO, Circuit Judges, and RESTANI*, Judge

JUDGMENT

This cause came on to be heard on the record from the United States District Court for the District of New Jersey and was argued on December 10, 2007.

On consideration whereof, it is now hereby ADJUDGED and ORDERED that the order of the District Court entered December 29, 2005, be and the same is hereby reversed. Costs taxed against the Appellee. All of the above in accordance with the opinion of this Court.

Attest:

/s/ Marcia M. Waldron
Clerk

DATED: April 8, 2008

*Hon. Jane A. Restani, Chief Judge, United States Court of International Trade, sitting by designation.

/

United States Court of Appeals,
Third Circuit.

Joseph C. COLACICCO, Individually and as Executor of the Estate of Lois Ann Colacicco, Deceased,
Appellant
v.
APOTEX INC.; Apotex Corp., as Subsidiary of Apotex, Inc.; Smithkline Beecham, d/b/a GlaxoSmithKline
Beth Ann McNellis, on Behalf of the Estate of Theodore DeAngelis, Deceased and in Her Own Right
v.
Pfizer Inc.; John Does 1-5; ABC Doe Corp.; DEF Doe Corp.; GHI Doe Corp.
Pfizer Inc., Appellant.
Nos. 06-3107, 06-5148.

Argued Dec. 10, 2007.
Filed April 8, 2008.

Before: SLOVITER, AMBRO, Circuit Judges, and RESTANI [FN*], Judge.

FN* Hon. Jane A. Restani, Chief Judge, United States Court of International Trade, sitting by designation.

OPINION OF THE COURT

SLOVITER, Circuit Judge.
The issue before us is one of preemption, an area of the law that need delicately balance federal interests and those of the states. It harks back to the very

beginning of our republic, and has continued to occupy us ever since. Preemption is not a doctrine that lends itself to a black-letter rule. One size does not fit all. The decision must be based on the circumstances presented in the particular situation.

The plaintiffs in these consolidated cases are the husband and daughter, respectively, of two adults who committed suicide after taking medication from the class of antidepressants known as selective serotonin reuptake inhibitors ("SSRIs"). The common question presented by the cases is whether the plaintiffs may maintain their state-law tort actions against the manufacturers of two such drugs on the theory that the drugs' labeling failed to warn of their association with an increased risk of suicidality. The central issue is whether actions taken by the Food and Drug Administration ("FDA") pursuant to its authority under the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301-397, and the corresponding regulatory scheme preempt the plaintiffs' state-law failure-to-warn claims.

I.

SmithKline Beecham, d/b/a GlaxoSmithKline ("GSK"), manufactures Paxil, an SSRI that is used to treat depression. On October 6, 2003, Lois Colacicco's physician prescribed Paxil for her depression. After her prescription was filled with a generic version of Paxil, Lois Colacicco began taking that medication. Less than a month later, on October 28, 2003, at the

age of fifty-five, she committed suicide in her New York home.

At the time of Lois Colacicco's death, the labeling for Paxil included the following language in its "Precautions" section:

> *Suicide:* The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for PAXIL should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose....

Colacicco App. at 436. Apotex, Inc. and Apotex Corp. (together, "Apotex") manufacture and distribute the generic version of paroxetine hydrochloride (the active ingredient in Paxil) ingested by Lois Colacicco. The labeling for Apotex's generic paroxetine was identical to GSK's labeling for Paxil.

After Lois Colacicco's death, her husband, Joseph C. Colacicco, filed suit against Apotex and GSK in the United States District Court for the Eastern District of Pennsylvania, alleging that those companies violated state common-law tort rules and New York state consumer protection laws by selling their products with labels that failed to warn consumers of the increased risk of emergent suicidality and worsening depression in adults taking paroxetine. On May 26, 2006, Apotex and GSK moved to have

Colacicco's complaint dismissed on the ground that it was preempted by federal law and, alternatively, that GSK did not owe a duty of care to the consumers of generic paroxetine, such as Lois Colacicco. The District Court dismissed the complaint on the basis of preemption. *Colacicco v. Apotex, Inc.*, 432 F.Supp.2d 514, 537-39 (E.D.Pa.2006).

Pfizer is the manufacturer of Zoloft, another SSRI that is used to treat depression. On January 22, 2003, sixty-four-year old Theodore DeAngelis was prescribed Zoloft for anxiety and depression. DeAngelis ingested that drug in the days leading up to his death by suicide on January 30, 2003. At the time of his death, the suicide precaution on Zoloft's labeling read as follows:

> *Suicide*-The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Close supervision of high risk patients should accompany initial drug therapy. Prescriptions for Zoloft (sertraline) should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose.

McNellis App. 499-500.

Following DeAngelis' death, Beth Ann McNellis, his daughter and the executrix of his estate, filed suit in New Jersey state court, alleging that Pfizer violated various New Jersey products liability and consumer fraud statutes by selling Zoloft without warning

consumers that it increased the risk of suicidality in those ingesting the drug. Pfizer removed the action to the United States District Court for the District of New Jersey and moved for summary judgment on the ground that McNellis' claim was preempted by federal law. The Court denied that motion on December 29, 2005. *McNellis ex rel. DeAngelis v. Pfizer, Inc.* ("*McNellis I* "), No. Civ. 05-1286(JBS), 2005 WL 3752269, at *13 (D.N.J. Dec.29, 2005). On September 29, 2006, following the dismissal of Colacicco's complaint in the Pennsylvania District Court, the New Jersey District Court denied Pfizer's motion to vacate its denial of the summary judgment motion, but certified its order for interlocutory appeal. The District Court framed the question for appeal as follows:

> Whether ... the United States Food and Drug Administration's requirements for the form and content of the labeling for the prescription antidepressant Zoloft preempted New Jersey's failure-to-warn law, under the doctrine of conflict preemption, where the FDA's regulations at 21 C.F.R. 201.57(e) [(2003)] and 314.70(c)(6)(iii) [(2007)] permit a manufacturer to unilaterally enhance its warning when the manufacturer has reasonable evidence of an association of a serious hazard with a drug.

McNellis ex rel. DeAngelis v. Pfizer, Inc. ("*McNellis II*"), No. Civ. 05-1286(JBS), 2006 WL 2819046, at *13 n. 9 (D.N.J. Sept.29, 2006). We must decide which of the two fine opinions authored by two of the ablest

district judges in this circuit most closely expresses our view of the difficult issue presented.

II.

The FDA is charged with "promot[ing] the public health by promptly and efficiently reviewing [drug manufacturers'] clinical research and taking appropriate action on the marketing of regulated products in a timely manner" and "protect[ing] the public health by ensuring that ... drugs are safe and effective." 21 U.S.C. § 393(b)(1), (b)(2)(B). In this capacity, the FDA regulates the introduction of all new drugs. *Id.*§ 355(a). Persons intending to market a drug must first file a new drug application ("NDA") with the FDA. *Id.*§ 355(b). An NDA must include, inter alia, full reports of investigations into the drug's safety and effectiveness, the components and production methods used to manufacture the drug, and "specimens of the labeling proposed to be used for such drug." *Id.*§ 355(b)(1); *see also*21 C.F.R. § 314.50(c)(2)(i) (requiring manufacturers to include "statements describing the reasons for omitting a section or subsection of the labeling format in § 201.57 of this chapter"), (e)(2)(ii).

Although "labeling" may be commonly understood as the label affixed to a prescription bottle, in this context it also encompasses the written material sent to the physician and included with the drug provided to the patient.[FN1] The FDA regulations require prescription drug labeling to include "a summary of the most clinically significant information ... critical

to safe use of the drug," including, inter alia, potential safety hazards associated with use of the drug. 21 C.F.R. § 201.57(a)(10), (c)(6)(i). Applicants must also include a "summary of the benefits and risks of the drug, including a discussion of why the benefits exceed the risks under the conditions stated in the labeling." *Id.*§ 314.50(d)(5)(viii).

> FN1. "Labeling" is defined by statute as "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." 21 U.S.C § 321(m). Thus, labeling "embraces advertising or descriptive matter that goes with the package in which the articles are transported,"*Kordel v. United States*, 335 U.S. 345, 350, 69 S.Ct. 106, 93 L.Ed. 52 (1948), in addition to any label that may be placed directly on a pill bottle.

The FDA must deny an NDA if it finds that:

> (1) the investigations [discussed above] do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof;
>
> (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; .... or
>
> (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular.

21 U.S.C. § 355(d). The FDA shall otherwise approve the NDA. *Id.* The "FDA will approve an application and issue the applicant an approval letter ... on the basis of draft labeling if the only deficiencies in the application concern editorial or similar minor deficiencies in the draft labeling." 21 C.F.R. § 314.105(b). However, "[s]uch approval will be conditioned upon the applicant incorporating the specified labeling changes exactly as directed, and upon the applicant submitting to FDA a copy of the final printed labeling prior to marketing." *Id.*

The FDA's post-approval oversight of drug labeling is governed primarily by regulation.[FN2] At the times relevant to this litigation, 21 C.F.R. § 201.56 described the general requirements for the content and format of drug labeling, while 21 C.F.R. § 201.57 set forth the specific requirements for such labeling.[FN3] Section 201.57(e) required manufacturers to "describe serious adverse reactions and potential safety hazards" under the heading "*Warnings.*" 21 C.F.R. § 201.57(e) (2003). Moreover, "[t]he labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." *Id.* The same section states that "[s]pecial problems, particularly those that may lead to death or serious injury, may be required by the [FDA] to be placed in a prominently displayed box.... If a boxed warning is required, its location will be specified by the [FDA]."*Id.*

FN2. Because many of the relevant regulations were revised or relocated after the dates relevant to this litigation (both DeAngelis and Lois Colacicco were prescribed SSRIs and committed suicide between January and October of 2003), we set forth the regulations in effect during that time period in the text and, where applicable, provide parallel citations to the current language and location of those regulations in footnotes. Unless otherwise noted, the substance of the regulations cited in this opinion have remained consistent between January of 2003 and the present.

FN3. As part of the FDA's amendments to its labeling regulations in 2006, additional labeling requirements for recently approved drugs were added to § 201.56 and that section was retitled. *See*21 C.F.R. § 201.56 (2007); *see also*71 Fed.Reg. 3922, 3986 (Jan. 24, 2006). Meanwhile, the specific requirements relating to drugs introduced prior to the amendments were amended and redesignated as § 201.80. *See*71 Fed.Reg. at 3988, 3996. Of primary importance to this litigation, the text formerly appearing at § 201.57(e) now appears at § 201.80(e). The relevant language remains unchanged. *Compare*21 C.F.R. § 201.57(e) (2003), *with*21 C.F.R. § 201.80(e) (2007). *See also*71 Fed.Reg. at 3996.

FDA regulations also govern the procedures for revising drug labeling. At all times relevant to this litigation, an applicant was required to notify the FDA of any changes to an approved drug, including its labeling, by one of three methods, depending on the magnitude of the intended change. *See*§ 314.70(a)-(d) (2003). Section 314.70(b) covered "supplements requiring FDA approval before the change is made." *Id.*§ 314.70(b). "Any change in labeling, except one described in [subsections] (c)(2) or

(d) of this section" required FDA pre-approval. *Id.*§ 314.70(b)(3)(i). Subsection (d) was limited to minor changes that may be submitted with the drug manufacturer's annual report, and is not implicated by this litigation. *See id.*§ 314.70(d). Subsection (c), however, described "changes that may be made before FDA approval." *Id.*§ 314.70(c). In particular, "[a]n applicant shall submit a supplement at the time the applicant makes" a change to its labeling "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction." *Id.*§ 314.70(c)(2)(i). The supplemental submissions by which § 314.70(c) changes are accomplished are sometimes referred to as "changes being effected" or "CBE" supplements.[FN4]

FN4. The FDA also amended § 314.70 in 2006. The regulation now refers to changes under subsections (b), (c), and (d) as "major," "moderate," and "minor" changes, respectively. 21 C.F.R. § 314.70(b), (c), (d) (2007). For the purposes of this litigation, subsections (b) and (d) are not materially different. Subsection (c), however, is now titled "Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (moderate changes)." *Id.* § 314.70(c). Nonetheless, that subsection also states that the FDA "may designate a category of changes for the purpose of providing that, in the case of a change in such category, the holder of an approved application may commence distribution of the drug product involved upon receipt by the agency of a supplement for the change." *Id.* § 314.70(c)(6). The listed categories include changes in labeling "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction." *Id.* § 314.70(c)(6)(iii)(A). Thus, for all practical purposes, subsection (c)(2)(i) has simply been relocated to subsection (c)(6)(iii)(A), but the FDA may determine that products incorporating such labeling changes may not be

distributed until the agency has received the CBE supplement or thirty days thereafter. Finally, the FDA now provides express notice that if it "disapproves the supplemental application, it may order the manufacturer to cease distribution of the drug product(s) made with the manufacturing change." *Id.* § 314.70(c)(7).

> After oral argument, the FDA submitted a proposed rule that would further limit the type of changes that may be effected pursuant to § 314.70(c)(6)(iii). *See*73 Fed.Reg. 2848 (Jan. 16, 2008). Specifically, that regulation would be limited to: "Changes in the labeling to reflect newly acquired information, except for changes to the information required in § 201.57(a) of this chapter (which must be made under paragraph (b)(2)(v)(C) of this section), to accomplish any of the following: (A) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under 201.57(c) of this chapter...."73 Fed.Reg. at 2853.

Drug manufacturers have continuing obligations to report adverse drug experiences, *id.*§ 314.80(c), and any "significant new information ... that might affect the safety, effectiveness, or labeling of the drug product,"*id.*§ 314.81(b)(2)(i). Failure to abide by these obligations may result in withdrawal of an approved drug. *Id.*§§ 314.80(j), 314.81(d).

Although regulations describe the particulars of the FDA's oversight of drug labeling, the FDCA describes the primary penalties for a drug manufacturer's failure to comply with those regulations. The FDA must withdraw approval of a drug if it finds "on the basis of new information before [it,] ... that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. § 355(e). The FDA may withdraw approval of a drug if, "on the basis of new information before [it,] ... the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the [FDA] specifying the matter complained of." *Id.*

The distribution of "misbranded" drugs is also prohibited by the FDCA. *Id.*§ 331(a), (b). A drug is misbranded if its "labeling is false or misleading in any particular,"*id.* § 352(a), if its labeling lacks "adequate warnings against use ... where its use may be dangerous to health,"*id.* § 352(f), or if "it is dangerous to health when used in the ... manner ... prescribed, recommended, or suggested in the labeling thereof,"*id.* § 352(j). The FDA has the authority to enforce the prohibition on misbranding by initiating injunction proceedings, *see id.* § 332, criminal prosecutions, *see id.* § 333(a), and the seizure of misbranded drugs, *see id.* § 334.

Once a drug has been approved, it is included in the FDA's published list of approved drugs. *See*21 U.S.C. § 355(j)(7). Such a drug is then referred to as a "listed drug." *Id.* § 355(j)(2)(A)(i). A listed drug is sometimes also referred to as an "innovator" or "pioneer" drug. *See, e.g., Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1494, 1497-98 (D.C.Cir.1996). Although the manufacturers of listed drugs, such as GSK and Pfizer in this case, are governed by all of the requirements associated with NDAs, the manufacturers of generic drugs, such as Apotex, are not required to submit an NDA. Rather, such manufacturers must abide by certain statutes and regulations that are based on the equivalence of generic drugs to the listed drugs.

The Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments) relaxed the approval procedures for generic drug manufacturers, allowing them to submit an abbreviated NDA ("ANDA"). Pub.L. No. 98-417, 98 Stat. 1585 (codified at 21 U.S.C. § 355(j), 35 U.S.C. §§ 156, 271, 281). An ANDA must contain information showing the generic drug's bioequivalency to the listed drug and that "the labeling proposed for the new drug is the same as the labeling approved for the listed drug...."21 U.S.C. § 355(j)(2)(A)(iv) & (v).[FN5] FDA regulations also provide that the agency may seek withdrawal of a generic drug, pursuant to notice and the opportunity for a hearing, if "the labeling for the [generic drug] is no longer consistent with that for the listed drug referred to in the [ANDA]."21 C.F.R. § 314.150(b)(10).

FN5. The FDA states that generic drug manufacturers may not add new warnings to the approved labeling for the listed drug. 57 Fed.Reg. 17,950, 17,953, 17,955, 17,961 (April 28, 1992).

III.

The District Courts had jurisdiction over the plaintiffs' claims under 28 U.S.C. § 1332. We have jurisdiction over Colacicco's appeal pursuant to 28 U.S.C. § 1291 following the entry of the order of the Pennsylvania District Court dismissing Colacicco's complaint; we have jurisdiction over Pfizer's appeal from the New Jersey District Court's interlocutory order denying Pfizer's motion for summary judgment in McNellis' case because the District Court certified that order pursuant to 28 U.S.C. § 1292(b).

[1] The issue underlying the District Courts' orders presents a question of law. We apply plenary review over their preemption determinations. See *Pennsylvania Employees Benefit Trust Fund v. Zeneca Inc.*, 499 F.3d 239, 242 (3d Cir.2007) (motion to dismiss); *Horn v. Thoratec Corp.*, 376 F.3d 163, 166 (3d Cir.2004) (motion for summary judgment).

IV.

[2] The doctrine of preemption is rooted in the Supremacy Clause, U.S. Const. art. VI, cl. 2, which provides that the "Constitution, and the Laws of the United States which shall be made in Pursuance thereof ... shall be the supreme Law of the

Land."Early in our constitutional history, the Supreme Court interpreted this language to invalidate state laws that "interfere with, or are contrary to," federal law, the genesis of the preemption doctrine. *Gibbons v. Ogden*, 22 U.S. (9 Wheat.) 1, 211, 6 L.Ed. 23 (1824). The Supreme Court has identified three major situations where there is preemption. They were described in *Hillsborough County v. Automated Med. Labs., Inc.* as: (1) "express" preemption, applicable when Congress expressly states its intent to preempt state law; (2) "field" preemption, applicable when "Congress' intent to pre-empt all state law in a particular area may be inferred [because] the scheme of federal regulation is sufficiently comprehensive" or " 'the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject;' " and (3) "conflict" preemption, applicable when "state law is nullified to the extent that it actually conflicts with federal law," even though Congress has not displaced all state law in a given area.[FN6] 471 U.S. 707, 713, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985) (quoting *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230, 67 S.Ct. 1146, 91 L.Ed. 1447 (1947)).

FN6. Both field and conflict preemption are sometimes referred to as forms of implied preemption. *See, e.g., Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 884, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000); *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287, 115 S.Ct. 1483, 131 L.Ed.2d 385 (1995). However, the Supreme Court has also asserted that these three categories are not "rigidly distinct;" for example, "field pre-emption may be understood as a species of conflict preemption: A state

> law that falls within a pre-empted field conflicts with Congress' intent (either express or plainly implied) to exclude state regulation." *English v. Gen. Elec. Co.*, 496 U.S. 72, 79-80 n. 5, 110 S.Ct. 2270, 110 L.Ed.2d 65 (1990).

An express preemption situation is exemplified by the Supreme Court's recent decision in *Riegel v. Medtronic, Inc.*, --- U.S. ----, 128 S.Ct. 999, 169 L.Ed.2d 892 (2008), where it considered the effect of the express preemption provision of the Medical Device Amendments of 1976 ("MDA") to the FDCA.[FN7] It held that in light of that provision, plaintiffs' claims that an arterial catheter was designed, labeled, and manufactured in a way that violated New York common law were preempted. *Id.* at 1003, 1005, 1011. *See alsoHorn*, 376 F.3d at 166.

> FN7. The statutory language provides that:
>
> > no State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement (1) which is different from, or in addition to, any requirement applicable under [the MDA] to the device, and (2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under [the Act].
>
> 21 U.S.C. § 360(k)(a).

In the *Colacicco* case, the Pennsylvania District Court noted that GSK and Apotex conceded that express and field preemption are not implicated, and proceeded exclusively under a conflict preemption analysis. 432 F.Supp.2d at 523. After reviewing the

applicable principles and relevant precedent, and according considerable deference to the FDA's position, the Court held that Colacicco's claims are preempted. *Id.* at 537-38. In so holding, the Court rejected Colacicco's argument that the FDA's position should not be accorded deference because it was inconsistent with the FDA's prior statements. The Court concluded that "after 2000, the FDA has been very consistent." *Id.* at 531-32.

A directly contrary conclusion was reached by the New Jersey District Court in the *McNellis* case. In the first of two opinions on the issue, the Court denied defendant Pfizer's motion for summary judgment, holding that it was unwilling to find that Congress intended to obviate the state laws upon which McNellis' complaint was based. *McNellis I,* 2005 WL 3752269, at *10. The Court held that discovery was needed on whether Pfizer had reasonable evidence of an association between Zoloft and suicidality. *Id.* at *11. In its opinion the following year, the Court declined to vacate its earlier opinion, and instead determined that "there can be no conflict preemption because the FDA's regulations do not conflict with New Jersey's failure to warn laws." *McNellis II,* 2006 WL 2819046, at *5. The Court held that the interpretation of the FDA was not entitled to the substantial deference accorded by the Pennsylvania District Court, and certified its order to this court for interlocutory appeal. *Id.* at *10, *13.

The pharmaceutical companies do not seriously argue that this is a case of express preemption [FN8] or field

preemption. We therefore limit our consideration to whether the plaintiffs' state-law claims conflict with the federal scheme.

> FN8. Apotex and GSK briefly argue that this is a case of express preemption because the 1962 Amendments to the FDCA stated: "Nothing in the amendments made by this Act to the [FDCA] shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such amendments and such provision of State law." Drug Amendments of 1962, Pub.L. No. 87-781, § 202, 76 Stat. 780, 793 (Oct. 10, 1962). Of course, the plain language of this provision states that the Amendments do not preempt state law in the absence of a conflict. Thus, to the extent that this provision affects our analysis, it merely states that conflict preemption applies. In other words, this "express preemption" provision simply leads us to a conflict preemption analysis, which may be applied independently of an express preemption analysis.

A.

[3] We consider first whether there is a presumption against preemption applicable in this case. The existence *vel non* of such a presumption is contested. The Supreme Court has stated: "[i]n all pre-emption cases, and particularly in those in which Congress has legislated in a field which the States have traditionally occupied, we start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress." *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996) (hereafter referred to as

"*Lohr* ") (citation, internal quotation marks, and alterations omitted). Colacicco and McNellis emphasize this "presumption against preemption," and both District Courts recognized the existence of that presumption. *See Colacicco,* 432 F.Supp.2d at 524; *McNellis I,* 2005 WL 3752269, at *3. Although a presumption against preemption is commonly acknowledged, the Supreme Court has made clear that the application of such a presumption is not always appropriate. *See Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341, 347-48, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001) (declining to apply a presumption against preemption where the plaintiff alleged fraud on the FDA).

Apotex and GSK argue that a presumption against preemption does not apply in the circumstances presented here because the states have not traditionally been involved in the regulation of drug labeling, whereas the federal government has regulated that area for over a hundred years. Pfizer takes an even broader position, arguing that the presumption against preemption does not apply at all in conflict preemption cases.[FN9] The Supreme Court's decision in *Hillsborough County* undermines both of these arguments. In that case, the Court stated that the "presumption that state or local regulation of matters related to health and safety is not invalidated under the Supremacy Clause,"471 U.S. at 715, 105 S.Ct. 2371, and then proceeded to analyze whether local regulations imposed on blood plasma centers "conflict with the federal scheme," *id.* at 720, 105 S.Ct. 2371. The Court concluded that the

County's ordinances and regulations, which imposed donor testing and requirements beyond those contained in the federal regulations, and which were designed to protect the health of the donors, to ensure the quality of the plasma, and to protect the recipients of the plasma, *id.* at 715-16, 105 S.Ct. 2371, were not preempted by the federal regulatory scheme because the County's requirements "do not imperil the federal goal of ensuring sufficient plasma,"*id.* at 722, 105 S.Ct. 2371.

> FN9. Pfizer also argues that it has overcome the presumption were it applicable. Where appropriate, we have not hesitated to find a conflict even after applying the presumption against preemption. *See Fasano v. Fed. Reserve Bank of New York*, 457 F.3d 274, 283, 290 (3d Cir.2006).

The Supreme Court later addressed the presumption against preemption in *Lohr*, where the plaintiff, who was injured by the failure of her pacemaker, filed a "common-law negligence action against the manufacturer of an allegedly defective medical device." 518 U.S. at 474, 116 S.Ct. 2240. The manufacturer argued that the claim was preempted by a provision in the MDA that bars state or local requirements different from those applicable under the MDA and which relate to the safety or effectiveness of any device covered by the Act.[FN10] *Id.* at 481, 116 S.Ct. 2240. The Court referred to the states' police powers to protect the health and safety of their citizens, *id.* at 485, 116 S.Ct. 2240, the premise of the presumption against preemption, in holding that plaintiff's negligence action was not

preempted. A plurality of the Court noted that the statutory language precluded any additional "requirement," not any "remedy," under state law, *id.* at 487, 116 S.Ct. 2240, and concluded, by reference to the legislative history, that the statute "was not intended to pre-empt most, let alone all, general common-law duties enforced by damages actions." *Id.* at 491, 116 S.Ct. 2240. We note, however, that the Court did not discuss the presumption against preemption in its recent opinion in *Riegel* considering the same provision of the MDA at issue in *Lohr*.

FN10. *See* supra note 7.

There are, as the pharmaceutical companies argue, relevant Supreme Court decisions where the Court explicitly declined to apply any presumption against preemption. In *Buckman,* plaintiffs, who claimed injuries from the use of orthopedic bone screws, brought suit against the consultant to the manufacturer on the theory that its statements defrauded the FDA and led the agency to approve a device that caused the plaintiffs' injuries. *See*531 U.S. at 343, 347-48, 121 S.Ct. 1012. The Supreme Court held that plaintiffs' fraud claims were preempted. It rejected plaintiffs' argument that there was a "virtually irrefutable presumption against implied preemption of private damage remedies predicated on an alleged conflict with a federal remedial scheme." *Id.* at 351, 121 S.Ct. 1012 (internal quotation marks omitted). Because "the relationship between a federal agency and the entity it regulates ... originates from, is governed by, and

terminates according to federal law," the Court concluded that the plaintiffs' claims did not implicate the traditional state interest in the regulation of public health and safety, and thus it did not apply the presumption against preemption. *Id.* at 347-48, 121 S.Ct. 1012.

Similarly, in *United States v. Locke,* 529 U.S. 89, 94, 108, 120 S.Ct. 1135, 146 L.Ed.2d 69 (2000), the Supreme Court considered whether Washington State laws governing oil tanker operations and designs enacted after the oil spill caused by the Exxon Valdez were preempted by a comprehensive federal regulatory scheme governing oil tankers. The Court declined to apply a presumption against preemption because the case concerned "national and international maritime commerce," a field in which "Congress has legislated ... from the earliest days of the Republic." *Id.* The Court noted that "an 'assumption' of nonpre-emption is not triggered when the State regulates in an area where there has been a history of significant federal presence." *Id.*

While the decisions in *Buckman* and *Locke* are distinguishable from the cases before us, they do make clear that it is "the purpose of Congress [as] the ultimate touchstone of pre-emption analysis,"*Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992) (citations, internal quotation marks, and alterations omitted), to which we must turn. *See alsoRice*, 331 U.S. at 230, 67 S.Ct. 1146; *Fasano v. Fed. Reserve Bank of New York*, 457 F.3d 274, 284 (3d Cir.2006).

Colacicco and McNellis argue that preemption is inappropriate because Congress has never expressed its intent to preempt state-law tort actions challenging drug labeling. McNellis notes that the New Jersey District Court concluded that it was "unwilling to find ... that Congress intended to obviate the very state laws that provide remedies to consumers harmed by dangerous products and deceptive marketing in the absence of a clear and compelling Congressional statement." *McNellis I*, 2005 WL 3752269, at *10 (citing *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 450, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005)).

The pharmaceutical companies respond by quoting the Supreme Court's statement that "in a situation where state law is claimed to be pre-empted by federal regulation, a 'narrow focus on Congress' intent to supersede state law [is] misdirected,' for '[a] pre-emptive regulation's force does not depend on express congressional authorization to displace state law.' " *City of New York v. FCC*, 486 U.S. 57, 64, 108 S.Ct. 1637, 100 L.Ed.2d 48 (1988) (quoting *Fid. Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 154, 102 S.Ct. 3014, 73 L.Ed.2d 664 (1982)). In fact, the Supreme Court has found that even where an express preemption saving clause demonstrated Congress' intent to exempt common-law tort actions from preemption, the language of the saving clause did not suggest an intent to "bar the ordinary working of conflict pre-emption principles" or preserve "state-law tort actions that conflict with federal regulations." *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 869, 120

S.Ct. 1913, 146 L.Ed.2d 914 (2000). The Court held that federal regulations may preempt common-law tort actions under a conflict preemption analysis despite a statutory provision stating that " '[c]ompliance with' a federal safety standard 'does not exempt any person from any liability under common law.' " *Id.* at 868, 120 S.Ct. 1913 (quoting 15 U.S.C. § 1397(k) (1988 ed.)). Thus, the Court concluded that plaintiff's tort action against the automobile manufacturer for failing to install airbags was preempted under conflict preemption principles although expressly saved from preemption by statute. *Id.* at 881, 120 S.Ct. 1913.

It follows that in this case, which is also one of conflict preemption, the lack of a Congressional directive expressly approving or rejecting preemption in the context of drug labeling regulations is not determinative. Rather, the conflict preemption analysis is designed to determine the propriety of preemption where Congress has not explicitly stated its intent. Seen in this light, Pfizer's argument that the presumption against preemption is inapplicable in the context of implied conflict preemption has more force. Although the Supreme Court applied the presumption in *Hillsborough County*, a decision in which it engaged in a conflict preemption analysis, that analysis followed the Court's consideration of field preemption principles. 471 U.S. at 716-20, 105 S.Ct. 2371.[FN11] Therefore, the extent to which the Court relied on the presumption in the context of its conflict analysis is not clear. Here, we recognize the applicability of the presumption against preemption,

but note the tension between such a presumption, which emphasizes the "clear and manifest purpose of Congress,"*Lohr*, 518 U.S. at 485, 116 S.Ct. 2240 (internal quotation marks omitted), and implied conflict preemption, which analyzes preemption in the absence of any explicit intent, *cf. Geier*, 529 U.S. at 885, 120 S.Ct. 1913 (failing to formally apply the presumption against preemption, but "assum[ing] that Congress or an agency ordinarily would not intend to permit a significant conflict").

> FN11. Although both field and conflict preemption are generally thought of as forms of implied preemption, a focus on Congressional intent is of greater value in the context of field preemption, where Congress' mere presence in a given field indiscriminately nullifies all state law in the field, than in the context of conflict preemption, which excludes state law only to the extent that it requires individuals to act contrary to conflicting federal obligations.

B.

[4] A conflict between state and federal law "arises when compliance with both federal and state regulations is a physical impossibility or when state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Hillsborough County*, 471 U.S. at 713, 105 S.Ct. 2371 (citations and internal quotation marks omitted); *see also City of New York*, 486 U.S. at 64, 108 S.Ct. 1637 ("The statutorily authorized regulations of an agency will pre-empt any state or local law that conflicts with such regulations or frustrates the purposes thereof.").

There are not many examples of instances where it is impossible to comply with both federal and state law, presumably because state legislatures and regulators do not readily seek confrontation with federal authority. One such example is provided by the Court's 1913 decision where it considered the effect of a 1907 Wisconsin statute providing that mixtures or syrups offered for sale "shall have upon them no designation or brand ... other than that required by the state law...."*McDermott v. Wisconsin*, 228 U.S. 115, 127, 33 S.Ct. 431, 57 L.Ed. 754 (1913). The federal food and drugs act passed in 1906 barred false and misleading labels on product packages. *Id.* at 127, 129, 33 S.Ct. 431. When the issue came before the Supreme Court, it stated that "the State may not, under the guise of exercising its police power or otherwise, ... enact legislation in conflict with the statutes of Congress passed for the regulation of the subject...."*Id.* at 131-32, 33 S.Ct. 431. The Court held that the state statute was invalid because "[t]he legislative means provided in the Federal law for its own enforcement may not be thwarted by state legislation having a direct effect to impair the effectual exercise of such means." *Id.* at 137, 33 S.Ct. 431.

The scarcity of actual conflict cases has led the Justices to pose hypothetical conflicts. In *Florida Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 143, 83 S.Ct. 1210, 10 L.Ed.2d 248 (1963), the Supreme Court hypothesized the existence of an impossibility conflict where "federal orders forbade

the picking and marketing of any avocado testing more than 7% oil, while the California test excluded from the State any avocado measuring less than 8% oil content." Under those circumstances, it would be a "physical impossibility" for avocado growers to comply with both federal and state law because California law would require them to do what federal law forbade, that is, pick their avocados after they surpassed the 7% ceiling established by federal law. *Id.*

In another case, where the issue was whether a federal statute that permits national banks to sell insurance in small towns preempts a state statute that forbids them to do so, Justice Breyer discussed the impossibility situation:

> In this case we must ask whether or not the Federal and State Statutes are in "irreconcilable conflict." The two statutes do not impose directly conflicting duties on national banks-as they would, for example, if the federal law said, "you must sell insurance," while the state law said, "you may not."

Barnett Bank of Marion County, N.A. v. Nelson, 517 U.S. 25, 31, 116 S.Ct. 1103, 134 L.Ed.2d 237 (1996).

Most of the preemption cases falling within the conflict category are cases that present the second scenario discussed in *Hillsborough County*-when "state law stands as an obstacle to the accomplishment and execution of the full purpose and objectives of Congress." 471 U.S. at 713, 105 S.Ct.

2371 (internal quotation marks omitted). In his opinion in *Barnett Bank,* Justice Breyer continued,

> the Federal Statute authorizes national banks to engage in activities that the State Statute expressly forbids. Thus, the State's prohibition of those activities would seem to "stan[d] as an obstacle to the accomplishment" of one of the Federal Statute's purposes-unless, of course, that federal purpose is to grant the bank only a very *limited* permission, that is, permission to sell insurance *to the extent that state law also grants permission to do so.*

517 U.S. at 31, 116 S.Ct. 1103 (quoting *Hines v. Davidowitz,* 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941)). After deciding that the McCarran-Ferguson Act antipreemption rule did not govern the case, *id.* at 38, 116 S.Ct. 1103, the Court held that the federal statute preempted the state statute, *id.* at 42, 116 S.Ct. 1103.

It is not only state statutes that may stand as obstacles to the achievement of federal objectives. It is now established that law suits based on state tort law, as well as on state statutes, may be viewed as presenting obstacles to the federal objectives and hence barred as preempted. In *Geier,* the Court held that an action against American Honda based on its failure to provide a driver's side airbag was preempted by a federal regulation. The Court adopted the principle that ordinary preemption principles apply to a state tort action where an actual conflict with a federal objective is at stake. *Geier,* 529 U.S. at

871-72, 120 S.Ct. 1913. The majority stated that in the absence of such a principle:

> state law could impose legal duties that would conflict directly with federal regulatory mandates, say, by premising liability upon the presence of the very windshield retention requirements that federal law requires. *See, e.g.*,49 CFR § 571.212 (1999). Insofar as petitioners' argument would permit common-law actions that "actually conflict" with federal regulations, it would take from those who would enforce a federal law the very ability to achieve the law's congressionally mandated objectives that the Constitution, through the operation of ordinary pre-emption principles, seeks to protect. To the extent that such an interpretation of the saving provision reads into a particular federal law toleration of a conflict that those principles would otherwise forbid, it permits that law to defeat its own objectives, or potentially, as the Court has put it before, to " 'destroy itself.' "

Id. (quoting *Am. Tel. & Tel. Co. v. Cent. Office Tel., Inc.*, 524 U.S. 214, 228, 118 S.Ct. 1956, 141 L.Ed.2d 222 (1998)).

A similar consideration was noted in *Lohr* where Justice Breyer, in his separate opinion concurring in part and dissenting in part, stated that "ordinarily, insofar as [federal law] pre-empts a state requirement embodied in a state statute, rule, regulation, or other administrative action, it would also pre-empt a similar requirement that takes the form of a standard

of care or behavior imposed by a state-law tort action." 518 U.S. at 504-05, 116 S.Ct. 2240. In *Horn*, which dealt with the same express preemption provision as in *Lohr*, we quoted from the FDA's letter brief stating, inter alia,

> State common law tort actions threaten the statutory framework for the regulation of medical devices, particularly with regard to FDA's review and approval of product labeling. State actions are not characterized by centralized expert evaluation of device regulatory issues. Instead, they encourage, and in fact require, lay judges and juries to second-guess the balancing of benefits and risks of a specific device to their intended patient population-the central role of FDA-sometimes on behalf of a single individual or group of individuals.

376 F.3d at 178.

State common-law tort actions based on the manufacturers' failure to warn present the pharmaceutical manufacturers with particular difficulties. State standards of care undoubtedly differ from state to state. Absent a determination that the FDA-approved labeling and the FDA's refusal to require the warnings suggested by plaintiffs in this case preempt state tort actions, the manufacturers may be subjected to considerable liability based on varying standards, with no benchmark that they should follow.

In holding the tort action based on the failure to provide airbags was preempted, the Court in *Geier* reviewed the history of the consideration of passive restraints by the federal agency, there the Department of Transportation. Similarly, in this case, before we can hold that a federal regulation or, as in *Geier*, the failure to regulate as extensively as plaintiffs sought, has preemptive force, we must review the record of the FDA's treatment of the desired warning at issue here.

[5] As discussed above, a new drug may not be marketed until it has received FDA approval. The FDA will not approve a drug if its "labeling is false or misleading in any particular." 21 U.S.C. § 355(d)(7). Even after a drug has been approved, a drug will be deemed misbranded if the "labeling is false or misleading in any particular" and the FDA may withdraw approval of that drug and prosecute the manufacturer. *See id.*§§ 331(b) (prohibition on misbranding), 355(e)(3) (withdrawal authority), 352(a), (f), (j) (definition of misbranding), 332 (injunction proceedings), 333(a) (criminal prosecutions), 334 (seizure). Thus, the FDCA vests the FDA with significant authority over drug labeling. FDA regulations further implement this authority.

Under its regulations, the FDA may withdraw approval of a drug if the manufacturer disregards its obligation to submit periodic reports notifying the FDA of adverse drug experiences and other new information that might affect the drug labeling. 21

C.F.R. §§ 314.80(c), (j), 314.81(b)(2)(i), (d). FDA regulations detail the information that must be included in the warnings section of drug labeling and instruct that such "labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug...."*Id.*§ 201.57(e) (2003); *id.*§ 201.80(e) (2007).

There are three distinct procedures by which manufacturers may revise their drugs' labeling, each of which requires the manufacturer to notify the FDA of its proposed revision. *See id.*§ 314.70(a)-(d). Generally, labeling changes require FDA pre-approval. *See id.*§ 314.70(b)(3)(i) (2003). However, changes that "add or strengthen a contraindication, warning, precaution or adverse reaction," may be implemented prior to the manufacturer's receipt of FDA approval. *Id.*§ 314.70(c)(2)(i) (2003); *id.*§ 314.70(c)(6)(iii)(A) (2007).

Colacicco and McNellis argue that because § 314.70(c) allows drug manufacturers to strengthen and augment warnings on drug labeling without prior FDA approval, the FDA labeling requirements constitute mere minimum standards for the information that may be required in their labeling. *See, e.g., Sprietsma v. Mercury Marine*, 537 U.S. 51, 58-59, 123 S.Ct. 518, 154 L.Ed.2d 466 (2002). Therefore, they argue that state-law failure-to-warn claims that would require manufacturers to strengthen or augment a warning do not conflict with FDA regulations, and are in fact complementary to those regulations.

The pharmaceutical companies respond that even though labeling changes made pursuant to § 314.70(c) do not require prior approval, the legality of those changes remains within the FDA's control. They state that because the FDA is directly involved with balancing the benefits and risks of a drug's labeling, *see, e.g.*,21 C.F.R. § 314.50(d)(5)(viii), and has the statutory authority to order the manufacturer to discontinue distribution of any products incorporating the manufacturer's labeling change, the FDA-approved labeling reflects the FDA's expert judgment about the information that must be included in a drug's labeling.[FN12]

> FN12. Apotex, for its part, argues that tort actions against generic drug manufacturers are preempted because the Hatch-Waxman Amendments and the FDA's implementing regulations require such manufacturers to maintain labeling identical to that of the innovator drug.

Of course, in this case we must focus on the effect of the FDA's failure to require a warning that plaintiffs argue was the cause of their injury rather than the effect of a positive regulation. It is always easier to evaluate the effect of a conflict created by a positive regulation than the effect created by inaction. It is difficult to know whether the absence of a regulation may reflect a wait-and-see approach or mere inertia. We are guided to some extent by *Geier* where the Court held that the failure of the Department of Transportation to require auto manufacturers to equip their 1997 vehicles with a specific form of passive restraint system, i.e. airbags, preempted the

state "no airbag" tort suit. 529 U.S. at 874, 881, 120 S.Ct. 1913.

In this case we need not speculate on the rationale of the FDA for its failure to require the adult suicidality warnings. Not only has the FDA filed an amicus brief in the *Colacicco* action but it has repeatedly rejected the scientific basis for the warnings that Colacicco and McNellis argue should have been included in the labeling. The FDA has actively monitored the possible association between SSRIs and suicide for nearly twenty years,[FN13] and has concluded that the suicide warnings desired by plaintiffs are without scientific basis and would therefore be false and misleading.

FN13. Colacicco, whose complaint was dismissed prior to discovery, argues that the District Court improperly relied on evidence of the FDA's past actions and that we are prohibited from considering that information. This problem does not arise in the McNellis case, which is before us following summary judgment proceedings. Of course, courts may place limited reliance on public records in the context of a motion to dismiss. *See Anspach ex rel. Anspach v. City of Philadelphia, Dep't of Pub. Health*, 503 F.3d 256, 273 n. 11 (3d Cir.2007). Thus, in *Anspach*, we took notice of FDA public records "not for the truth of [their] contents, but rather as evidence of the information provided by the federal government" to the relevant regulated parties. *Id.* Our recognition of the records contested here, all of which are publicly available, is similarly limited. *See also Jean Alexander Cosmetics, Inc. v. L'Oreal USA, Inc.*, 458 F.3d 244, 256 n. 5 (3d Cir.2006) (recognizing that courts may take judicial notice of prior judicial proceedings).

In 1991, after considering whether antidepressants caused or intensified suicidal thoughts, the FDA's Psychopharmacological Drugs Advisory Committee concluded that no such warning should be added to Prozac (an SSRI similar to Paxil and Zoloft) or other antidepressants. The FDA specifically rejected citizen petitions in 1991, 1992, and 1997 which sought to either withdraw approval of Prozac as a result of its asserted association with suicide or to include a suicide warning on the labeling of that drug. In each instance, the FDA concluded that there was insufficient evidence to take the actions requested.

DeAngelis committed suicide on January 22, 2003. The FDA approved the Zoloft suicide precaution seven separate times before and after that date, in each instance requiring Pfizer to market the drug with the precise labeling approved.[FN14] Further, just months before DeAngelis' death, the FDA filed an amicus brief in an action before the Court of Appeals for the Ninth Circuit, stating that it had concluded that there was no scientific basis for a warning suggesting that Zoloft causes suicidality. *See* Brief for the United States as Amicus Curiae, *Motus v. Pfizer Inc.*, 358 F.3d 659 (9th Cir.2004) (Nos.02-55372, 02-55498), 2002 WL 32303084 (brief submitted September 10, 2002).[FN15]

FN14. The FDA first approved Zoloft for the treatment of depression in adults on December 30, 1991, conditioning its approval on Pfizer's incorporation of specifically indicated labeling revisions. In 1996, the FDA approved Zoloft for a new indication, the treatment of obsessive compulsive disorder ("OCD"), with that approval again conditioned on Pfizer's incorporation of a series of labeling revisions. The FDA proceeded to approve the use of Zoloft for panic disorder and pediatric OCD in 1997, post-traumatic stress disorder in 1999,

premenstrual dysphoric disorder in 2002, and, on February 7, 2003, social anxiety disorder. Each time the FDA approved Zoloft for a new indication, it required that the final printed labeling be identical to the labeling attached to the FDA's approval.

FN15. The New Jersey District Court acknowledged the FDA's position in *Motus*, but decided that it was not appropriate to defer to that litigation position. See *McNellis I*, 2005 WL 3752269, at * 10. However, we distinguish between the agency's legal position in its amicus brief and its factual representations. In the *Motus* brief, the FDA stated not just its legal conclusions with respect to the applicability of preemption, but it also reported its view of the state of scientific research regarding Zoloft and antidepressants at that time. The FDA's summary of its scientific determinations must be distinguished from the agency's construction of a statute, as the review of scientific information is strictly within its expertise. The FDA asserted facts in support of its legal position, and we take notice of its statement of those facts, rather than its legal position.

The FDA also repeatedly approved the Paxil labeling in effect at the time of Lois Colacicco's prescription of Paxil on October 6, 2003, and her death on October 28, 2003, approving it for a new indication, the treatment of generalized anxiety disorder, just a year before those events.[FN16] The FDA approved Apotex's application to market generic paroxetine on June 30, 2003, concluding that "the drug is safe and effective for use as recommended in the submitted labeling," which included the suicide precaution discussed above, rather than a warning. See Letter from Gary Buehler, Director, Office of Generic Drugs, Center for Drug Evaluation and Research, FDA, to Apotex Corp. 3 (July 30, 2003), *available at* http:// www.

fda.gov/cder/foi/appletter/2003/75356ap.pdf (last visited January 8, 2008). Significantly, on June 19, 2003, the FDA issued a public statement to address reports associating the pediatric use of Paxil with suicidality, in which it stated: "There is no evidence that Paxil is associated with an increased risk of suicidal thinking in adults." FDA Talk Paper, FDA Statement Regarding the Anti-Depressant Paxil for Pediatric Population (June 19, 2003), *available at* http:// www. fda. gov/ bbs/ topics/ answers/ 2003/ ans 01230. html (last visited Nov. 8, 2007).

> FN16. As with its approvals of Zoloft, the FDA approved Paxil for new indications on the condition that the final drug labeling be identical to the labeling approved by the FDA. *See, e.g.*, Letter from Russell Katz, M.D., Director, Division of Neuropharmacological Drug Products, Office of Drug Evaluation I, Center for Drug Evaluation and Research, FDA, to GlaxoSmithKline (Oct. 2, 2002), *available at* http:// www. fda. gov/ cder/ foi/ appletter/ 2002/ 20031 se8-035ltr.pdf (last visited January 8, 2008).

On October 27, 2003, the FDA issued a Public Health Advisory regarding increased suicidality in pediatric users of antidepressants. This advisory was limited to pediatric patients; a warning for adult patients was not issued. In that advisory, the FDA announced that it would continue to research the reports of suicidality in pediatric patients treated with antidepressants, explaining that "[s]uch reports are very difficult to interpret, in the absence of a control group, as these events also occur in untreated patients with depression." FDA, FDA Public Health Advisory (Oct. 27, 2003), *available at* http:// www. fda. gov/ cder/

drug/ advisory/ mdd. htm (last visited January 8, 2008).

Thus, even when it began to reevaluate its position regarding the association of antidepressants with pediatric and adolescent suicidality, the FDA continued to announce its rejection of adult suicidality warnings for SSRIs as it had for the decade before the prescriptions and deaths at issue in this litigation. Just months prior to Lois Colacicco's death, the FDA publicly stated that Paxil was not associated with a risk of suicidality in adults. Similarly, four months before DeAngelis' death, the FDA filed a public brief stating its position that scientific evidence did not support the addition of a suicide warning on Zoloft's labeling.

Although preemption is commonly thought of in terms of statutes and regulations, a federal agency's action taken pursuant to statutorily granted authority may also have preemptive effect over state law. *See Chicago & N.W. Transp. Co. v. Kalo Brick & Tile Co.*, 450 U.S. 311, 327, 101 S.Ct. 1124, 67 L.Ed.2d 258 (1981) ("These findings by the [Interstate Commerce] Commission, made pursuant to the authority delegated by Congress, simply leave no room for further litigation over the matters respondent seeks to raise in state court."); *NCNB Texas Nat'l Bank v. Cowden*, 895 F.2d 1488, 1497-99 (5th Cir.1990) (finding that Federal Deposit Insurance Corporation's action taken pursuant to statutory authority preempted state law); *cf. Sprietsma*, 537 U.S. at 66-67, 123 S.Ct. 518

(recognizing that an agency's refusal to regulate may be construed as a determination that no such regulation is appropriate and have preemptive force). Because the standard for adding a warning to drug labeling is the existence of "reasonable evidence of an association of a serious hazard with a drug,"21 C.F.R. § 201.57(e), and the FDCA authorizes the FDA to prohibit false or misleading labeling, a state-law obligation to include a warning asserting the existence of an association between SSRIs and suicidality directly conflicts with the FDA's oft-repeated conclusion that the evidence did not support such an association. Therefore, under the circumstances of this case, the plaintiffs' failure-to-warn claims are preempted by the FDA's actions taken in accordance with its statutory authority.

The FDA clearly and publicly stated its position prior to the prescriptions and deaths at issue here. Therefore, we need not decide whether preemption would be appropriate under different facts-such as where the FDA had not rejected the substance of the warning sought or where the FDA only stated its position after a lawsuit had been initiated-or under the broader theories of preemption argued by the parties. Thus, we do not decide whether the FDA's mere approval of drug labeling is sufficient to preempt state-law claims alleging that the labeling failed to warn of a given danger, whether FDA approval of drug labeling constitutes minimum standards in the absence of the FDA's express rejection of a specific warning, or whether actions against generic drug manufacturers are preempted on

the basis of their obligations under the Hatch-Waxman Amendments.[FN17] Our holding is limited to circumstances in which the FDA has publicly rejected the need for a warning that plaintiffs argue state law requires. *Cf. Dowhal v. SmithKline Beecham Consumer Healthcare*, 32 Cal.4th 910, 12 Cal.Rptr.3d 262, 88 P.3d 1, 11 (2004) (concluding that an FDA "letter established a federal policy prohibiting defendants from giving consumers any warning other than the one approved by the FDA in that letter, and that the use of a [warning required by state law] would conflict with that policy").

> FN17. In contrast to our decision, the Supreme Court of Vermont has held that plaintiffs' negligence and failure-to-warn claims alleging inadequate warnings on the labeling of an anti-nausea drug "did not conflict with the FDA's labeling requirements for [the drug] because [Wyeth] could have warned against [the danger alleged by plaintiffs] without prior FDA approval, and because federal labeling regulations create a floor, not a ceiling, for state regulation." *Levine v. Wyeth*, 944 A.2d 179, ¶ 6 (Vt.2006), *cert. granted*,--- U.S. ----, 128 S.Ct. 1118, 169 L.Ed.2d 845 (2008). The Vermont Court found that there was "no evidence that the FDA intended to prohibit defendant from strengthening the [drug] label pursuant to [§] 314.70(c)" and thus it was not impossible for Wyeth to comply with both state and federal obligations. *Id.* ¶ 23. The facts in these cases are otherwise.

The plaintiffs raise two primary objections to this conclusion. First, they argue that nothing less than the FDA's explicit rejection of a drug manufacturer's request to add a contested warning to its drug labeling should suffice to establish conflict preemption. Second, they contend that the

pharmaceutical companies failed to provide the FDA with sufficient information for it to make a valid decision regarding the necessity of a suicidality warning. Neither argument is persuasive.

As we previously noted, the FDA is authorized by statute to reject an NDA if the labeling is false or misleading in any particular and may withdraw its approval of a drug upon the same findings. *See*21 U.S.C. § 355(d)(7), (e)(3). Plaintiffs argue, however, that the FDA's actions were insufficient to manifest such a rejection here. They ask us to overlook the FDA's various public statements rejecting the existence of an association between SSRIs and adult suicidality because they were not made in the context of the FDA's formal rejection of a CBE supplement submitted by one of the defendant pharmaceutical companies.

We agree that a court could more easily determine the preemption issue if the FDA had formally rejected such a CBE supplement, but we cannot compel the defendant companies to suggest a CBE supplement that they believe is unnecessary. Nor do we favor encouraging regulated parties to submit CBE supplements for the sole purpose of insulating themselves from potential liability. *Cf.* 44 Fed.Reg. 37,434, 37,435 (June 26, 1979) (cautioning, in the context of medical malpractice liability, that "it would be inappropriate to require statements in drug labeling that do not contribute to the safe and effective use of the drug, but instead are intended solely to influence civil litigation in which the agency

has no part"). Thus, we reject the notion that, in order to rise to the level of a conflict in this situation, the FDA's rejection of a warning must be imbued with the formality proposed by the plaintiffs.

Colacicco further argues that the FDA's failure to require an adult suicidality warning cannot be seen as a rejection of the warning that his lawsuit would require because "GSK manipulated or withheld information from the FDA."Colacicco Reply Br. at 9. This contention borders on the charge that GSK defrauded the FDA by manipulating or withholding such information. *Cf. Buckman,* 531 U.S. at 346-47, 121 S.Ct. 1012. Such a claim, if supported by sufficient evidence, should be brought before the FDA. As far as we know from the record, Colacicco has not done so.

In the New Jersey action, McNellis opposed Pfizer's motion for summary judgment by submitting copies of research studies that were made public, which McNellis argued showed a link between SSRIs and suicidality. McNellis does not argue that the FDA was unaware of this material. Our focus is on the period before the two deaths that are the subject of the actions before us. We note, however, that the FDA has continued its close scrutiny of the effect of SSRI drugs on suicidality of adults. In March of 2004, the FDA directed GSK and nine other manufacturers of SSRIs to include stronger warnings on drug labels about the need to monitor adult patients for signs of worsening depression or suicidality, but noted that it had "not concluded that these drugs cause worsening

depression or suicidality in adult patients." [FN18] Br. for the United States as Amicus Curiae at 13 (citing FDA Talk Paper, FDA Issues Public Health Advisory on Cautions for Use of Antidepressants in Adults and Children (March 22, 2004), *available at* http:// www. fda. gov/ bbs/ topics/ ANSWERS/ 2004/ ANS 01283. html).

> FN18. In April 2006, GSK, after reviewing studies that disclosed a higher incidence of suicidal behavior in young adults treated with Paxil, modified its Paxil label to include a warning that young adults "especially those with [major depressive disorder], may be at an increased risk of suicidal behavior when treated with" Paxil. Br. for the United States as Amicus Curiae at 14 (citing Paxil Label, *available at* http:// us. gsk. com/ products/ assets/ US paxil.pdf (last visited Feb. 27, 2008)). It made this change only after filing the proposed change with the FDA and waiting the required 30 days.

More recently, the FDA, after its review of the aggregated data from all SSRI manufacturers, reaffirmed its conclusion that there is insufficient evidence demonstrating that SSRIs are associated with adult suicidality. In its widely distributed notice on Antidepressant Use in Children, Adolescents and Adults dated May 2, 2007, *available at* http: //www. fda. gov/ cder/ drug/ antidepr essants/ default. htm (last visited Feb. 22, 2008), the FDA incorporated its conclusions that "[s]hort-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24" and that adults ages 65 and older taking antidepressants have a decreased risk of suicidality. Revisions to Product Labeling, *available at* http://

www. fda. go· cder/ drug/ anti depressants/ antidepress ants_ label_ change_ 2007. pdf (last visited Feb. 22, 2008); *see also* FDA News, FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications, http:// www. fda. gov/ bbs/ topics/ NEWS/ 2007/ NEW 01624. html (May 2, 2007).[FN19] The FDA Revisions to Product Labeling directed the drug companies (including manufacturers of Paxil and Zoloft) to make changes in the warnings included at the beginning of the package inserts that confirm that antidepressants increase the risk of suicidality in children, adolescents, and young adults but that the studies did not show an increase in the risk of suicidality in adults older than age 24.[FN20] In light of the FDA's continued review of existing scientific studies, we reject plaintiffs' arguments that the FDA lacked information that would have dissuaded it from rejecting an adult suicidality warning for Zoloft, Paxil, or generic paroxetine in 2003.

FN19. We may, of course, take judicial notice of this development "which [took] place after the judgment appealed from." *Werner v. Werner*, 267 F.3d 288, 295 (3d Ci: 2001).

FN20. The entire text of the revised warning reads as follows:

> Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Insert established name] or any other antidepressant in a child, adolescent, or young adult

> must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Insert Drug Name] is not approved for use in pediatric patients. [The previous sentence would be replaced with the sentence, below, for the following drugs: Prozac: Prozac is approved for use in pediatric patients with MDD and obsessive compulsive disorder (OCD). Zoloft: Zoloft is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD). Fluvoxamine: Fluvoxamine is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD).] (See Warnings: Clinical Worsening and Suicide Risk, Precautions: Information for Patients, and Precautions: Pediatric Use).
>
> Revisions to Product Labeling, *available at* http:// www. fda. gov/ cder/ drug/ antidepr essants/ anti depressants_ label_ change_ 2007. pdf (last visited Feb. 22, 2008).

[6] The FDA has taken the position, both in the preamble to the 2006 amendments revising the drug labeling regulations and in its amicus brief in the *Colacicco* case, that plaintiffs' claims are preempted as a result of the actions taken by the FDA pursuant to its regulatory authority. The preamble specifically

states that preemption applies to "claims that a [manufacturer] breached an obligation to warn by failing to include a statement in labeling or in advertising, the substance of which had been proposed to FDA for inclusion in labeling, if that statement was not required by FDA at the time plaintiff claims the [manufacturer] had an obligation to warn." 71 Fed.Reg. 3922, 3936 (Jan. 24, 2006). The FDA explains in the amicus brief that "the basis for federal preemption is not the [labeling] guidelines themselves ..., but rather FDA's repeated determinations prior to October 2003 that there was insufficient scientific evidence of an association between adult use of SSRI and suicide or suicidality to permit a warning on the labeling for those drugs...." Br. for the United States as Amicus Curiae at 28.

We would ordinarily be leery of an agency's view of what is essentially a legal issue, but we note that in *Geier* the Supreme Court recently addressed the weight to be given to an agency's position on preemption. The Court "place [d] some weight" on a Department of Transportation interpretation, as set forth in an amicus brief, of a rule that it had promulgated. *Geier*, 529 U.S. at 883, 120 S.Ct. 1913. The Court considered that Congress had delegated the agency "authority to implement the statute; the subject matter is technical; and the relevant history and background are complex and extensive." *Id.* The Court stated that the agency was " 'uniquely qualified' to comprehend the likely impact of state requirements." *Id.* (quoting *Lohr*, 518 U.S. at 496,

116 S.Ct. 2240). The Court also noted the consistency of the agency's position over time, *id.*, and the coherence of the agency's views, *id.* at 885, 120 S.Ct. 1913. Although the Court did not rely solely on the agency's position, it noted that "a specific expression of agency intent to pre-empt, made after notice-and-comment rulemaking" was not necessary to find conflict preemption. *Id.*

[7] From *Geier*'s discussion of an agency's informal position regarding preemption, we conclude (1) that an agency's position concerning preemption need not be contained in a formal regulation in order to be considered, and (2) that such a position is subject to a level of deference approximating that set forth in *Skidmore v. Swift & Co.*, 323 U.S. 134, 65 S.Ct. 161, 89 L.Ed. 124 (1944). *Cf. Christensen v. Harris County*, 529 U.S. 576, 587, 120 S.Ct. 1655, 146 L.Ed.2d 621 (2000) (quoting *Skidmore*, 323 U.S. at 140, 65 S.Ct. 161) (holding that agency interpretations contained in statements that "lack the force of law" are " 'entitled to respect' " only to the extent they have the " 'power to persuade' ").[FN21]

FN21. Counsel for GSK suggested that a combination of *Skidmore* and *Auer* deference was appropriate. Under *Auer v. Robbins*, 519 U.S. 452, 461, 117 S.Ct. 905, 137 L.Ed.2d 79 (1997) (citations and internal quotation marks omitted), an agency's interpretation of its own regulation is "controlling unless plainly erroneous or inconsistent with the regulation." However, because the FDA purports to interpret both the statutory structure and regulatory framework, we believe it more prudent to apply *Skidmore* deference, which is the weaker of the two. This is also consistent with *Geier*, wherein the Court

> considered an agency's interpretation of its own regulation under a less deferential standard than that suggested by *Auer*. 529 U.S. at 883, 120 S.Ct. 1913.

"The fair measure of deference to an agency administering its own statute has been understood to vary with circumstances, and courts have looked to the degree of the agency's care, its consistency, formality, and relative expertness, and to the persuasiveness of the agency's position." *United States v. Mead Corp.*, 533 U.S. 218, 228, 121 S.Ct. 2164, 150 L.Ed.2d 292 (2001) (alterations omitted) (citing *Skidmore*, 323 U.S. at 139-40, 65 S.Ct. 161).

It is important to consider the rationale given by the agency for its position that its actions preempt state law in the particular situation. In the case of the SSRI drugs at issue, Paxil, Zoloft, and the generic paroxetine manufactured by Apotex, the FDA has explained that "[u]nder-use of a drug based on dissemination of unsubstantiated warnings may deprive patients of efficacious and possibly lifesaving treatment. Further, allowing unsubstantiated warnings would likely reduce the impact of valid warnings by creating an unnecessary distraction and making even valid warnings less credible." Br. for the United States as Amicus Curiae at 16-17. The FDA's view that "the imposition of liability under state law for defendants' alleged failure to warn *would* interfere with FDA's accomplishment of regulatory objectives,"*id.* at 22, is in our view entitled to at least as much deference, if not more, as the FDA's view of its preemption authority. The Pennsylvania District Court accorded the FDA's views "significant"

deference, *Colaciccio*, 432 F.Supp.2d at 529, and we agree that in at least this respect the FDA's view is entitled to some degree of deference.

In light of the circumstances in this case, we agree that the FDA's rejection of the warning plaintiffs proffer preempts a state-law action premising liability on a drug manufacturer's failure to include such a warning in the drug labeling notwithstanding that the agency's view was not subject to notice-and-comment rulemaking.

The Supreme Court has recently acknowledged the FDA's expertise in the context of the medical devices covered by the MDA. It stated, "[b]ecause the FDA is the federal agency to which Congress has delegated its authority to implement the provisions of the Act, the agency is uniquely qualified to determine whether a particular form of state law 'stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress,' and, therefore, whether it should be pre-empted." *Lohr*, 518 U.S. at 496, 116 S.Ct. 2240 (citing *Hines*, 312 U.S. at 67, 61 S.Ct. 399). Justice Breyer, concurring in that decision, also noted that the Court has "suggested that, in the absence of a clear congressional command as to pre-emption, courts may infer that the relevant administrative agency possesses a degree of leeway to determine which rules, regulations, or *other administrative actions* will have pre-emptive effect." *Id.* at 505, 61 S.Ct. 399 (Breyer, J., concurring) (emphasis added) (citing cases). Of course, the FDA is equally expert, if not more so, with respect to

regulation of drugs, with which it has had a longer experience than with medical devices.

We need not decide whether the FDA's position in this case is inconsistent, as plaintiffs argue, with the FDA's 2000 rule proposal. We see no inconsistency between the FDA's preamble to the 2006 amendments and its long-held position that it has the responsibility to determine whether a warning is required. *Compare*44 Fed.Reg. at 37,447 (stating, in 1979, that "the decision as to whether a warning is legally required for the labeling of a drug must rest with the agency"), *with*71 Fed.Reg. at 3934 ("In fact, the determination whether labeling revisions are necessary is, in the end, squarely and solely FDA's under the act.").

In conclusion, based on our own review of the FDCA, the FDA's regulations, and the FDA's actions taken pursuant to its statutory authority, we conclude that the failure-to-warn claims brought by Colacicco and McNellis conflict with, and are therefore preempted by, the FDA's regulatory actions. It is important to note that we express no view as to the merits of the issue whether SSRIs contribute to adult suicidality. We are not scientists and we do not purport to have any expertise on that issue. That is within the FDA's authority. This decision is based on the record before us.

V.

For the above-stated reasons, we will affirm the judgment of the United States District Court for the Eastern District of Pennsylvania dismissing Colacicco's complaint and we will reverse the order certified by the United States District Court for the District of New Jersey with instructions that judgment be entered in favor of the defendants. In light of our decision with respect to preemption, we need not reach the other issues considered by the District Courts.

AMBRO, Circuit Judge, dissenting.

The majority opinion describes these cases as situations calling for preemption: the expert agency, the Food and Drug Administration ("FDA"), consults scientific data to generate the optimal warnings (not too lax, not too alarmist) for drug labels-and state tort lawsuits would disrupt this fine system. But there is an important contrary view that has prevailed until recently: state tort law complements FDA provisions on drug warnings, in part by eliciting more information than the FDA would glean otherwise from pharmaceutical manufacturers. This contrary view has, I believe, the better argument in terms of legal doctrine on preemption, congressional intent, and the history of state tort law alongside federal law. Although the majority opinion is well-crafted and responsibly narrow, I would not move even the short distance my colleagues go toward preemption of state-law torts. I thus respectfully dissent.

I. Presumption Against Preemption

The majority opinion begins its analysis where I would, by examining whether we are to apply a presumption against preemption. State tort law, dealing with failure-to-warn claims (like those brought by the plaintiffs in our cases), addresses health and safety and thus falls within the states' traditional police powers. *See Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996) (describing the presumption against preemption and asserting "the historic primacy of state regulation of matters of health and safety"). As the majority recognizes, the presumption does not always apply; for example, it does not apply to claims alleging fraud on the FDA. *See Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 347-48, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001). That the presumption there does not apply-where common sense points to federal law governing exclusively those who seek to defraud a federal agency-is no surprise, and hardly weakens the presumption when it does apply.

The presumption against preemption must inform our analysis of both "whether Congress intended any pre-emption at all" and "the scope of its intended invalidation of state law." *Lohr*, 518 U.S. at 485, 116 S.Ct. 2240 (emphasis omitted). When the presumption applies, rebutting it requires a clear expression that Congress intended to preempt. *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005) ("In areas of traditional

state regulation, we assume that a federal statute has not supplanted state law unless Congress has made such an intention clear and manifest.") (citations and internal quotation marks omitted).

In my view, the majority opinion under-emphasizes congressional intent as the "ultimate touchstone of pre-emption analysis." *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992) (citations and internal quotations marks omitted). Our inquiry is "guided" by a focus on gaining " 'a fair understanding of *congressional purpose.*' " *Lohr*, 518 U.S. at 485-86, 116 S.Ct. 2240 (quoting *Cipollone*, 505 U.S. at 530, 112 S.Ct. 2608) (emphasis in original). As the majority opinion rightly recognizes, the defendants in our cases do not make a serious argument that this case involves express preemption or field preemption. But I would place more significance on the fact that the key *conflict* preemption cases that the majority opinion relies on involve express statutory preemption provisions. *Geier v. American Honda Motor Company*, 529 U.S. 861, 864-65, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000) (evaluating viability of state-tort-law claims in light of a preemption provision, 15 U.S.C. § 1392(d), and a savings provision, *id.*§ 1397(k), within the National Traffic and Motor Vehicle Safety Act of 1966); *Lohr*, 518 U.S. at 481, 116 S.Ct. 2240 (evaluating viability of state-tort-law claims in light of the preemption provision of the Medical Devices Act, 21 U.S.C. § 360k(a)).

Even when considering a species of implied preemption-as conflict preemption generally is, *see Geier*, 529 U.S. at 884, 120 S.Ct. 1913-we should be asking whether Congress intended to preempt. In our cases, we have no statutory preemption provision to interpret that relates to drug labeling in the Food, Drug and Cosmetic Act ("FDCA"). This fact should push us to hold the presumption against preemption in place, as we lack the best kind of evidence of congressional intent: statutory text.

The absence of a relevant preemption provision in the FDCA does not, of course, resolve whether the presumption against preemption is overcome by something else. The Supreme Court has "held repeatedly that state laws can be pre-empted by federal regulations as well as by federal statutes." *Hillsborough County v. Automated Med. Labs.*, 471 U.S. 707, 713, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985). Although initial approval of drug labeling involves both statutory and regulatory provisions, FDA regulations primarily govern the continuing oversight of drug-label revisions. These regulations, at the time relevant to this litigation, required drug manufacturers to revise labeling "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug,"21 C.F.R. § 201.57(e), and to submit supplemental information in the event that they "add or strengthen a contraindication, warning, precaution, or adverse reaction,"*id.*§ 314.70(c). The defendants in our cases rely primarily on their continuing obligations under

these FDA regulations for their conflict-preemption argument.

Yet the mere presence of a comprehensive regulatory scheme such as the FDA's for drug labeling does not itself unseat the presumption against preemption. *Hillsborough County,* 471 U.S. at 717, 105 S.Ct. 2371 ("We are even more reluctant to infer pre-emption from the comprehensiveness of regulations than from the comprehensiveness of statutes.").[FN22] Because our focus must remain on congressional intent, we should remember in deciding questions of *regulatory* preemption that any inferences regarding congressional purpose typically will be indirect. Congress enacted the FDCA, which in turn enabled the FDA to adopt its regulations regarding continuing (*i.e.*, post-approval) drug labeling. To overcome the presumption against preemption, the defendants in our cases must show that Congress implicitly intended to allow the FDA to adopt regulations that preempt failure-to-warn lawsuits under state law. *Cf. Fidelity Federal Sav. & Loan Ass'n v. de la Cuesta,* 458 U.S. 141, 162, 102 S.Ct. 3014, 73 L.Ed.2d 664 (1982) (holding that Federal Home Loan Bank Board regulations preempted state law where "the statutory language suggests that Congress expressly contemplated, and approved, the Board's promulgation of regulations superseding state law" after also inquiring into the Board's own intent to preempt).

FN22. The majority opinion suggests that, because *Hillsborough County* considered field preemption in analyzing the municipal ordinances at issue, the

operation of the Supreme Court's application of the presumption against preemption in that case "is not clear." I disagree with this suggestion. *Hillsborough County*'s discussion of the presumption against preemption appears in Part III of that opinion. 471 U.S. at 714-16, 105 S.Ct. 2371. The field-preemption analysis in Sections IV.A and IV.B, and the conflict-preemption analysis in Section IV.C, follow. *Id.* at 716-20, 105 S.Ct. 2371. In my view, the Court's purpose in setting out the presumption against preemption in Part III was to indicate that the presumption should guide the analysis in all sections of Part IV.

The majority opinion closes its discussion of the presumption against preemption by describing a "tension" between the presumption as outlined in *Lohr* and some seemingly contrary language in *Geier*.

But the *Geier* side of this doctrinal tug-of-war has slippery footing. The quoted language-"[O]ne can assume that Congress or an agency ordinarily would not intend to permit a significant conflict,"*Geier*, 529 U.S. at 885, 120 S.Ct. 1913-appears as a *dictum* in the context of a larger discussion of whether an agency must adopt a clear statement of preemptive intent for a conflict between federal regulation and state law to exist.[FN23] This sentence does not create a counter-presumption in favor of preemption, for the very next sentence in *Geier* states that "a court should not find pre-emption too readily in the absence of clear evidence of a conflict." *Id.* That is a restatement of the presumption against preemption, suggesting that we should not interpret *Geier* to muddy the presumption or to dilute its effect. [FN24]

FN23. That discussion in *Geier* settles the issue: an agency need not do so for a conflict to exist. 529 U.S. at 884-85, 120 S.Ct. 1913. Even without express statutory preemption or a clear agency statement on preemption, a court may find that state law "actual[ly] conflict[s]" with federal law under the facts of a particular case. *Id.* at 884, 120 S.Ct. 1913 (quoting *English v. Gen. Elec. Co.*, 496 U.S. 72, 79, 110 S.Ct. 2270, 110 L.Ed.2d 65 (1990)). I address the broader issue of how much deference we owe an agency's position on preemption below. *See infra* Part II.

FN24. In contrast, the majority opinion never again mentions the presumption against preemption after Section IV.A of its opinion, suggesting that the presumption is performing virtually no analytical work.

When a federal court undertakes a conflict-preemption analysis, a "significant conflict" between federal and state law might be the kind of "clear evidence" that could rebut the presumption against preemption. *Geier,* 529 U.S. at 885, 120 S.Ct. 1913. We can assume Congress or the FDA had awareness of products-liability law when legislating or regulating. So if we find a genuine conflict, we may conclude that Congress intended to preempt state law. But in situations involving less obvious conflicts, the presumption against preemption will be more difficult to overcome.

I would apply the presumption against preemption here. The plaintiffs' failure-to-warn claims stand near the heart of the states' police powers over matters of health and safety. And the existence and detailed nature of the federal scheme does not change our imperative to require clear congressional intent

(whether expressed directly in a preemption provision or implied by an authorizing statute enabling an agency to act) to preempt state tort law.

II. Deference to the FDA's View on Preemption

At the end of its conflict-preemption analysis-even after addressing the plaintiffs' arguments-the majority opinion considers the FDA's own view regarding the preemptive effect of its drug-labeling regulations. In 2006, the preamble to an FDA revision of its drug-labeling regulations stated that failure-to-warn claims are preempted if, at the time of injury, the substance of the alternative warning proposed by plaintiffs (1) had already been submitted to the FDA and (2) had not been adopted. 71 Fed.Reg. 3922, 3936 (Jan. 24, 2006). The FDA also filed an *amicus* brief in the *Colacicco* case before us, arguing that "federal law preempts a state tort claim arising out of drug manufacturers' alleged failure to provide a warning that FDA determined was not scientifically supported." FDA Br. 16. The FDA emphasizes that it strives for the optimal strength of warning. Anything less *or more* than the FDA-approved and FDA-monitored warning, in the agency's view, would be "false or misleading." *See*21 U.S.C. §§ 331(a)-(b), 352(a); Br. of *Amicus Curiae* United States at 2.

We must decide what weight we should give to these FDA views before analyzing the purported conflict in this case. I agree with the majority opinion that we should apply *Skidmore* deference to the FDA's informal position contained in its 2006 preamble and

its *amicus* brief in *Colacicco*. *See Geier*, 529 U.S. at 883, 120 S.Ct. 1913 (placing "some weight" on the Department of Transportation's interpretation of its own airbag regulation); *Skidmore v. Swift & Co.*, 323 U.S. 134, 139, 65 S.Ct. 161, 89 L.Ed. 124 (1944) (giving the Department of Labor's "interpretive bulletin" regarding the calculation of working hours a level of deference based on "all those factors which give it power to persuade, if lacking power to control"). The formulation in *Mead*, which cites *Skidmore* and which the majority opinion quotes, designates the following factors for consideration: "the degree of the agency's care, its consistency, formality, and relative expertness, and to the persuasiveness of the agency's position." *United States v. Mead Corp.*, 533 U.S. 218, 228, 121 S.Ct. 2164, 150 L.Ed.2d 292 (2001).

I disagree with the majority opinion, however, in its application of the standards articulated in *Skidmore* and *Mead*.Comparing FDA statements from 1979 and 2006, my colleagues discern "no inconsistency" between them.[FN25] I suggest a better analysis of inconsistency would take a more detailed view of the FDA's position(s) during the 27 intervening years.[FN26]

For instance, only slightly more than seven years ago the FDA disavowed any "federalism implications" or preemptive effect of changes to its requirements for prescription drug labeling. 65 Fed.Reg. 81,082, 81,103 (Dec. 22, 2000). Rather than maintaining a consistent position, the FDA now undertakes a "180-degree reversal." David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt*

Failure-to-Warn Claims, 96 Geo. L.J. 461, 474 n. 59 (2008) (internal quotation marks omitted). Its current position is novel rather than longstanding. *See id.* at 462 ("For most of its seventy-seven-year history [since receiving the name "Food and Drug Administration" in 1930], the [FDA] has regulated the drugs sold in the United States without any significant interaction with the world of state-law damages litigation."). I thus conclude that the FDA's position regarding preemption deserves little deference by way of its inconsistency.

FN25. Importantly, the majority opinion's quote from the 1979 regulation is taken out of context. Rather than contemplating the FDA's relation to state courts, the quoted sentence discusses the FDA's relation to panels of experts from which the agency seeks advice: "Although FDA often refers questions of whether a warning should be included in the labeling of a drug *to its standing advisory committees,* the decision as to whether a warning is legally required for the labeling of a drug must rest with the agency." 44 Fed.Reg. 37,434, 37,447 (June 26, 1979) (emphasis added). Thus there is no support I can find in the record for the proposition that, in 1979, the FDA viewed its drug-labeling regulations as preemptive of state tort law.

FN26. Some Supreme Court cases suggest that inconsistency is no bar to deference. *See, e.g., Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.,* 463 U.S. 29, 103 S.Ct. 2856, 77 L.Ed.2d 443. 42 (1983). But others have language suggesting that inconsistency counts against the agency's position. *See, e.g., Bates,* 544 U.S. at 449, 125 S.Ct. 1788 (finding a preemption argument "particularly dubious" in light of the EPA's change in position within five years).

The majority opinion relies on another of the *Skidmore* and *Mead* factors: agency expertise. Undoubtedly, the FDA has special expertise in evaluating the scientific evidence on pharmaceuticals' safety and efficacy. That expertise should contribute to any consideration of the proper mix of legal institutions used to regulate drug labeling. But, as my colleagues note, "[w]e would ordinarily be leery of an agency's view of what is essentially a legal issue." The FDA is not an expert on federalism concerns. Nor is the agency the only Government institution that should bring its perspective to bear on the relationship between the executive branch and state courts; Congress, federal courts, and state courts each have a constitutional responsibility under the Supremacy Clause to evaluate such issues. Thus, I would consider the FDA's expertise only a mild positive in our calculation of how much deference to apply in these cases.

The remaining factors listed in *Mead* weigh against giving the FDA's view on preemption much deference. With respect to "formality," the FDA has not engaged in notice-and-comment rulemaking on this issue, instead promulgating its views in a preamble to a regulation and a series of *amicus* briefs in cases like these. As the majority notes, notice-and-comment rulemaking is not *required* to find conflict preemption. *See Geier*, 529 U.S. at 885, 120 S.Ct. 1913. But the lack of notice-and-comment rulemaking should, all else equal, reduce the level of deference we give the FDA's position. Similarly, the lack of institutional formality suggests a relatively

low "degree of care" taken to outline its reasoning.[FN27]

In my view, a high degree of care on issues of preemption would involve scholarly, scientific, and public-health [FN28] research into the complex matters of law and policy that these cases implicate. I see no evidence in the record that the FDA conducted or commissioned independent research of this nature in preparing the 2006 preamble.

> FN27. By making this point I do not mean to criticize FDA counsel's efforts in writing its *amicus* brief in this case or at oral argument. On the contrary, counsel performed admirably in both regards. My focus here is in-depth institutional research on law and policy preceding the recent "about face" on agency preemption.
>
> FN28. A group of public health researchers writes that "[i]ndirect regulation of the pharmaceutical industry by tort litigation is an important complement to the regulation of drug safety by the FDA."Br. of *Amicus Curiae* Curt D. Furberg, M.D., Ph.D., *et al.* at 6. This view-based on various scholarly, peer-reviewed articles-does not receive any attention in the 2006 preamble or in the FDA's *amicus* brief. Notice-and-comment rulemaking would provide a forum for such research to be considered, but, as noted, the FDA has not undertaken that administrative process on the issue of preemption of state tort law.

In summary, the *Mead* factors counsel us to give the FDA's position a relatively low level of deference. The ultimate test under *Skidmore* is nonetheless whether the FDA's (and the defendants') view has the "power to persuade," 323 U.S. at 139, 65 S.Ct. 161, an evaluation I take up in Part III.

III. Conflict Preemption.

The defendants' argument is that labeling that satisfies the FDA is both the minimum and the maximum amount of labeling they may do. Under this view, the FDA believes it has struck the proper balance between safety and efficacy, that is, between avoiding unintended injuries to patients because of insufficient warnings while not deterring too many patients from using drugs that would benefit them because of unjustified over-warnings. Adding additional warnings unsupported by medical evidence would subject the defendants to FDA sanctions for false labeling. Conflict preemption must apply to block state-law claims for failure to warn, according to the defendants, since stronger warnings for Paxil and Zoloft-the drugs within the category of selective serotonin reuptake inhibitors ("SSRIs") involved in these cases-would violate FDA regulations. This makes it impossible, defendants continue, for them to have complied with both state and federal law. Alternatively, imposing an overlay of tort liability would frustrate the federal objective of having the FDA strike the safety-efficacy balance.

For the reasons I describe below, I disagree with this characterization of the interaction of FDA regulation and state tort law. Informed by the presumption against preemption, I see the federal and state constructs as complementary, as they have been since

the 1930s. The majority opinion's holding of preemption in these cases, despite an apparently narrow construction, threatens the institutional framework we have for balancing safety and efficacy in the pharmaceutical industry while compensating victims of wrongful injuries.

A. Absence of an Actual Conflict

None of the drug manufacturers in these cases attempted to enhance a warning and received an FDA sanction in response. The majority opinion correctly states that hypothetical conflicts can give rise to conflict preemption. But the hypothetical in question must be convincing for us to allow this. The conflict the defendants raise relies, at its heart, on the FDA punishing drug manufacturers for over-warning. But a heightened warning would likely have its source in new information that the FDA had not previously known. Thus, I find it hard to believe that, if a drug manufacturer augmented its warning in response to or in anticipation of a state tort lawsuit, the FDA would sanction the manufacturer for over-warning consumers under 21 U.S.C. §§ 331(a)-(b) and 352(a).

Indeed, drug manufacturers have authority to strengthen warnings without advance permission from the FDA. The plain language of 21 C.F.R. § 314.70 permits unilateral additions to warnings, subject to subsequent FDA approval: "[T]he holder of an approved application may commence distribution of the drug product involved upon receipt by the agency of a supplement for the change," including

such changes as "add[ing] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction." 21 C.F.R. §§ 314.70(c)(6), (c)(6)(iii)(A). The motivation for additional warnings, which the regulation does not address, need not come from inside the pharmaceutical company in question or FDA prodding. In particular, that motivation may come from a failure-to-warn lawsuit or the threat of one.

Drug manufacturers have the best information about the safety of their products. The FDA does not conduct its own drug trials and "does not have sufficient authority to require additional clinical trials after drug approval." Mary J. Davis, *The Battle Over Implied Preemption: Products Liability and the FDA*, 48 B.C. L.Rev. 1089, 1149 (2007). Thus, to avoid discouraging the party with the best safety information from coming forward, 21 C.F.R. § 314.70 permits a manufacturer to alter a drug label before the FDA has evaluated and approved the change.

The defendants and the FDA do not cite even one example of the FDA punishing a drug manufacturer for over-warning. *See* Oral Argument Tr. 82, Dec. 10, 2007 (statement of FDA counsel that she was "not aware of any instance" in which the FDA "told a manufacturer who added an increased warning that that warning was unsubstantiated and caused the drug to be misbranded").[FN29] At oral argument, counsel for GlaxoSmithKline mentioned that, in 2004, the FDA required additional language in response to a strengthened warning by Wyeth Pharmaceuticals in

a "changes being effected" supplement under 21 C.F.R. § 314.70. Merely requiring a clarification of or addition to warning language does not strike me as close to being close to a true conflict. On the contrary, the Wyeth example shows that the FDA typically engages in a back-and-forth discussion with drug manufacturers about warnings. In the event of a state tort lawsuit resulting in a warning that conflicted with the FDA's previous judgment, a commonplace dialogue between the manufacturer and the FDA could produce a warning complying with both federal regulations and state tort law.

> FN29. The majority opinion emphasizes a different fact: that the FDA, in response to citizen petitions and approvals of new uses for existing SSRIs, considered requiring a strengthened warning and declined. I agree that inaction of this kind is a form of agency action. But more important to me is that the FDA may never have sanctioned a drug manufacturer that strengthened a warning without prior FDA approval. This additional example of FDA inaction suggests that the conflict complained of is not an actual conflict.

B. Harmony Between Tort Law and FDA Regulation

Tort law and FDA regulation do not have conflicting goals. Both seek to strike a safety-efficacy balance. Under a negligence standard, most state courts balance the cost of care owed to a patient against the prospective harm. *See, e.g., La Russa v. Four Points at Sheraton Hotel*, 360 N.J.Super. 156, 821 A.2d 1168, 1173-74 (2003) (quoting Judge Learned Hand's formula from *United States v. Carroll Towing Co.*, 159 F.2d 169, 173,*reh'g denied*,160 F.2d 482 (2d

Cir.1947), which compares the cost of precautions with the expected loss); *cf.* Stephen G. Gilles, *On Determining Negligence: Hand Formula Balancing, The Reasonable Person Standard, and the Jury*, 54 Vand. L.Rev. 813, 816-22 (2001) (describing widespread use of, as well as complications in applying, the Hand formula).

Properly understood, the cost of additional warnings includes the consequences of over-warning that the defendants emphasize and that the FDA similarly takes into account.[FN30] In reaching its holding of conflict preemption, the majority focuses on the hypothetical scenario of differing (and presumably conflicting) results of the FDA regulatory process and state tort lawsuits. Because we are dealing with hypothetical situations, however, I would focus on the essential harmony of the standards applied by the FDA and state courts rather than the disharmony conjured about the results. Both institutions seek to balance safety and efficacy. If it turns out those results actually conflict, then it is time for Congress to step in or at least for the FDA to propose a rule followed by public comment before proclaiming preemption.

FN30. Advocates of preemption in these cases point to the danger of "over-warning" and imply that over-warning will result from jury decisions biased toward plaintiffs. Br. of *Amicus Curiae* Product Liability Advisory Council, Inc. at 14-23. This argument assumes that juries do not understand that the cost of care, including the cost of taking too much care, is part of determining negligence. I presume, for the purposes of analyzing a hypothetical conflict between federal and

> state law, that state-court judges will properly instruct juries about the negligence standard.

Allowing multiple institutions to investigate the difficult question of how strong to make a warning can have important benefits. State courts provide a check on agency power. Our society relies on the FDA to an enormous degree to monitor the safety of pharmaceuticals. But the FDA's toolkit is imperfect and incomplete by design. The FDA relies on the information provided by drug manufacturers (to repeat, it does no independent testing), and will always lack the inside perspective on clinical trials and data analyses stemming from those trials. Moreover, the FDA is limited as to the additional clinical trials it may require post-approval, Davis, *supra,* at 1149 & n. 444, and even "the reporting process for postapproval adverse reaction events ... is too weak,"*id.* at 1149 & n. 443. Also, as they play their parts in the post-approval process the drug manufacturer and the FDA will not necessarily ask the right questions. The citizen-petition administrative process was used here unsuccessfully to seek an FDA requirement of stronger warnings for SSRIs. Discovery in state tort lawsuits provides a different way for third parties to raise questions about new and existing drugs. Given this context, I would not eliminate the potentially valuable information-gathering tools of state tort law.

To make all this real, I would point out that the regulatory process at the FDA, even if it allows for submission of citizen petitions, does not compensate

the families of alleged victims like Lois Colacicco and Theodore DeAngelis. The availability of damages in state tort lawsuits can give injured citizens the incentive to come forward and share potentially valuable information. Even if an injury or death turns out not to have been caused by a drug or an insufficient warning, that information, too, can have social value. And the prospect of paying damages can sharpen drug manufacturers' incentives to place appropriate weight on safety as they strike the safety-efficacy balance. We should not lightly assume this balance now preempted-and by a single recently adopted preamble at that.

C. Backdoor Federalization

The FDA's position in these cases is an instance of "backdoor federalization," a descriptive term commentators have recently used to describe a trend in the federal courts toward finding state law preempted. On the positive side, centralized federal control can facilitate uniform regulation of a national market (like that for pharmaceuticals) and prevent states from interfering with the affairs of other states. Samuel Issacharoff & Catherine M. Sharkey, *Backdoor Federalization*, 53 UCLA L.Rev. 1353 (2006).

Unfortunately, the trend toward federalization is not fully benign. While the FDA seeks to keep private plaintiffs out of state court (or federal court applying state law in diversity actions), a separate line of jurisprudence has limited private rights of action.

There is a "troublesome" contrast in the way courts now tend to "grant agencies expansive discretion to interpret or declare the preemptive scope of the regulations they promulgate, whereas agencies are not given corresponding latitude to infer private rights of action under those same regulations." Catherine M. Sharkey, *Preemption by Preamble: Federal Agencies and the Federalization of Tort Law,* 56 DePaul L.Rev. 227, 258-59 (2007).

Although the FDA should have a strong voice in the debate among government institutions about preemption of state tort law, by executive order it must consult with state and local governments about the consequences of its regulations. *See id.* at 252-55 (citing Exec. Order No. 13,132, 64 Fed.Reg. 43,255, 43,257 (Aug. 10, 1999)). But nothing in the record suggests a dialogue between federal and state officials has occurred regarding preemption of failure-to-warn lawsuits.

I would interpret the absence of an express preemption statute, the text of the actual FDA regulations, and the late arrival of the FDA's statement on preemption in a preamble, as evidence that state tort law is not displaced. Tort lawsuits can generate useful information that the FDA can inject into its regulatory process. And tort damages can aid the FDA in aligning drug manufacturers' incentives to find the right balance between safety and efficacy. In any event, the choice to preempt state tort law is best left to Congress, should it wish to do so. In these

cases, I do not see the kind of conflict that implies Congress has made that choice.

IV. Conclusion

The plaintiffs allege that SSRIs increase the risk of patients committing suicide. They further allege that the drug manufacturers knew or should have known this, but failed to label their products appropriately. The defendants would have us halt any inquiry into their alleged negligence before it starts. They contend that, in the area of drug labeling, state tort law renders compliance with federal provisions impossible, or at least stands as an obstacle to federal objectives.

The FDA, which relies on information provided by others, seeks to stop one avenue of information-that gathered from suits under state tort law theories. But should an earlier series of FDA decisions indicating that the previous warnings were adequate, when they might be inadequate, preclude the operation of state tort law? The majority suggests that the plaintiffs' claims border on claiming fraud on the FDA. But the underlying issue in these preemption cases is the structure of federal-state relations. We must decide whether the FDA will be the sole decision-maker. Without a clear statement from Congress or clear evidence that state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress,"*Hines v. Davidowitz*, 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941), I am

reluctant to say that the defendants' claim of a conflict has scaled the presumption against preemption.

A holding of no preemption in these cases would not suggest in any way that the defendant drug manufacturers should be liable for plaintiffs' injuries. Like my majority colleagues, I express no view regarding the relationship between SSRIs and adult suicide. Allowing the plaintiffs' cases to proceed beyond the motion-to-dismiss stage means instead that the state courts and federal district courts applying state tort law may evaluate-provide a check on-whether the FDA struck the right balance in the precautions and warnings it required for SSRIs.

To review the history of this issue, the FDA has for over three-quarters of a century viewed state tort law as complementary to its warning regulations. Only for the last two years has it claimed otherwise. This "sea change," Sharkey, *supra*, at 242, in the FDA's conception of the relationship between federal and state law has not appeared in a regulation subject to notice and comment, but in a preamble to a regulation. With this background, I believe courts should fear to tread where Congress has not given us a clear statement. Because I see sound legal and policy reasons to hold that the presumption against preemption is not overcome, I would allow the plaintiffs' suits to go forward. I respectfully dissent.

United States District Court,E.D. Pennsylvania.
Joseph C. COLACICCO, Plaintiff,
v.
APOTEX, INC., et al., Defendants.
Civil Action No. 05-5500.

May 25, 2006.

MEMORANDUM

BAYLSON, District Judge.

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I. Introduction

Presently before this Court are two Motions to Dismiss, pursuant to F.R. Civ. P. 12(b)(6), filed separately by Defendants Apotex, Inc. and Apotex Corp. ("Apotex") and Defendant GlaxoSmithKline ("GSK").

The threshold issue presented by these motions is preemption-whether regulations of a federal agency, promulgated pursuant to a federal statute, and implementing that statute, require the Court to dismiss this pharmaceutical products liability suit based on common law tort principles alleging that inadequate labeling of a prescription drug led to the suicide of Plaintiff's wife.

The answer is "yes"-when Congress passed the Federal Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 355(a), the law which gives the Food and Drug Administration ("FDA") control over the regulation of the prescription drug industry, it vested the FDA with authority to regulate the specifics of drug labeling, making important judgments of what is required for safety of the consuming public, what new drugs may appear in the marketplace, and what warnings their instructions and labels must carry. The analysis that follows will reveal many conflicting court decisions on this topic. Fundamentally, a series of Supreme Court decisions point this Court in the direction of deference, and require dismissal of this case. Accordingly, both Defendants' motions to dismiss will be granted.

II. Background

A. Procedural Background

Plaintiff Joseph Colacicco ("Plaintiff") filed his original complaint on October 21, 2005, alleging the suicide death of his wife, Lois, resulted from the Defendant drug manufacturers' failure to warn of the increased risk of suicidal behavior linked to the anti-depressant Paxil and/or its generic equivalent. On

November 22, 2005, Defendant GSK filed its Motion to Dismiss (Doc. No. 5) ("Def. GSK Mem."). Plaintiff filed a Response (Doc. No. 9) on December 20, 2005, and GSK filed a Reply brief (Doc. No. 11) on December 27, 2005. Defendant Apotex filed a Motion to Dismiss (Doc. No. 10) on December 26, 2005 ("Def. Apotex Mem."), to which Plaintiff responded on February 7, 2006 (Doc. No. 19). By letter dated March 2, 2006, this Court asked counsel to answer questions that arose from its review of the briefs to date. All parties responded on March 13, 2006.(See Doc. No. 26 by Plaintiff, Doc. No. 27 by Defendant GSK, and Doc. No. 28, by Apotex) ("Supp. Mem."). Oral argument was held on March 17, 2006, at which Plaintiff's counsel withdrew Count I (breach of express warranty). On March 22, 2006, we again asked counsel by letter to answer additional questions that had surfaced, to which counsel responded on March 27, 2006 (See Doc. No. 33 by Apotex, Doc. No. 34 by GSK, and Doc. No. 38 by Plaintiff) ("2nd Supp. Mem."). Plaintiff filed an Amended Complaint on March 24, 2006 (Doc. No. 32), which asserted in Count III (fraud and violation of consumer protection law against GSK only) what had in the original complaint been plead as two counts against both Defendants-Count III (fraud) and Count X (violation of consumer protection law).[FN1] Both Defendants GSK and Apotex filed a Response to the Amended Complaint and Supplemental Brief in Support of their Motions to Dismiss, on March 31, 2006 (Doc. Nos. 39 and 40, respectively), and Plaintiff filed a memorandum in opposition to the renewed motions to dismiss on April 6, 2006 (Doc. No. 41). ("3rd Supp. Mem."). Then, due to the novel preemption issues presented in this case, the Court requested that the FDA file an *amicus* brief, which it did on May 10,

2006 (Doc. No. 45). *See* Brief for United States as *Amicus Curiae* Supporting Defendants, *Colacicco v. Apotex,* Civ. No. 05-5500, Doc. No. 45 (E.D.Pa. May 10, 2006) ("Colacicco Amicus"). Finally, the parties each submitted a response to the *amicus* brief on May 17, 2006 (Docs. No. 48, 49, 50) ("4th Supp. Mem.").

FN1. As Plaintiff's counsel withdrew Count I (breach of express warranty) on the record at the March 17, 2006 oral argument, the Court understands the Amended Complaint to omit that count as well.

B. Allegations in the Complaint

According to the Complaint, Plaintiff's wife, Lois Ann Colacicco, complained to her oncologist on October 6, 2003 of mild fatigue and depression. She was prescribed Paxil,[FN2] an anti-depressant drug manufactured by Defendant GSK. Soon thereafter, she began taking the generic version of the drug, paroxetine hydrochloride, which is a bio-equivalent of Paxil and manufactured by Defendant Apotex.[FN3] On October 28, 2003, after twenty-two days of ingesting the drug, Lois Colacicco committed suicide in her home.

FN2. The medical records do not indicate whether Lois' physician prescribed Paxil or its generic version; however, it is undisputed that she actually took the generic version.

FN3. The FDA approved Apotex's application to produce the generic form of Paxil on June 30, 2003.

Paxil is one of a class of drugs known as Selective Serotonin Reuptake Inhibitors ("SSRIs"), which are prescribed for the treatment of depression and anxiety. Plaintiff alleges that despite ample peer-

reviewed scientific literature published from the mid-1990s onward linking SSRIs to an increased risk of suicidality, at the time of Plaintiff's decedent's death the FDA-approved label did not warn of an association between Paxil (manufactured by GSK) and/or its generic equivalent (manufactured by Apotex) and suicidality. [FN4]

> FN4. The FDA recently retreated from its longstanding position that no linkage existed associating suicidality in adults with SSRI antidepressants, including Paxil. On June 30, 2005, the FDA issued a public health advisory warning of the potential for antidepressant medications to cause suicidal thoughts and behavior in adults. FDA Public Health Advisory, *Suicidality in Adults Being Treated with Antidepressant Medications*, June 30, 2005, *available at* http://www.fda.gov/cder/drug/advisory/SSRI200507.htm. The FDA is currently engaged in a comprehensive scientific review of existing studies to determine whether there is an increased risk of suicidal behavior in adults treated with antidepressant drugs. *Colacicco Amicus* at 11. On May 11, 2006, citing the results of a clinical study of nearly 15,000 patients treated with both Paxil and placebos, GlaxoSmithKline warned doctors via a letter that Paxil may raise teen suicide risk. *See* Associated Press, *FDA Warns of Suicide Risk for Paxil*, May 12, 2006, *available at* http://hosted.ap.org/dynamic/stories/P/PAXIL_SUICIDE_RISK?SITE=COBOU&SECTION=HOME&TEMPLATE=DEFAULT.

Plaintiff filed suit against both Defendants GSK and Apotex, asserting the liability of either or both based on a failure-to-warn theory. Plaintiff contends the warnings, which were disseminated to doctors and the public by GSK, were inadequate to inform adult users of the risk of suicide associated with the drug. He asserts the labeling was prepared solely by Defendant GSK and copied verbatim by Defendant

Apotex, which was required as part of the process to obtain approval from the federal FDA to manufacture the generic version of the drug. Alternately, Plaintiff asserts Defendant Apotex manufactured the drug which caused Lois Colacicco's death, and failed to warn adult users of the risk of suicide posed by the drug.

III. Jurisdiction and Legal Standard

A. Jurisdiction

This Court has diversity jurisdiction over this complaint pursuant to 28 U.S.C. § 1332 because the matter in controversy exceeds $75,000 and is between citizens of different states. Plaintiff is a resident of New York. Defendant GSK is a citizen of Pennsylvania. Defendant Apotex is citizen of Florida and Canada.

Venue is appropriate in this district, pursuant to 28 U.S.C. § 1391 because a substantial part of the events or omissions giving rise to Plaintiff's claims occurred in Pennsylvania or were intended to have consequences in Pennsylvania.

B. Legal Standard

When deciding a motion to dismiss pursuant to F.R. Civ. P. 12(b)(6), the court may grant the motion only if, accepting all well-pleaded allegations in the complaint as true, and viewing them in the light most favorable to plaintiff, the plaintiff is not entitled to relief. *Doug Grant, Inc. v. Greate Bay Casino Corp.*, 232 F.3d 173, 183 (3d Cir.2000). Accordingly, a federal court may dismiss a complaint for failure to

state a claim only if it is clear that no relief could be granted under any set of facts that could be proved consistent with the allegations. *Doe v. Delie,* 257 F.3d 309, 313 (3d Cir.2001).

C. Applicable State Law

As a federal court sitting in diversity, *Erie R.R. Co. v. Tompkins,* 304 U.S. 64, 58 S.Ct. 817, 82 L.Ed. 1188 (1938), requires that we apply the substantive law of the forum state. *Id.* at 78-80, 58 S.Ct. 817. Pursuant to a joint stipulation of all parties, Pennsylvania is the appropriate forum state, and thus the law of Pennsylvania will be applied to Counts I-II, and IV-IX, as well as the fraud portion of Count III of Plaintiff's Complaint. *See* Exhibit A, Joint Stip. of the Parties at p. 2 ¶ 1.[FN5] Count III also asserts a violation of the New York Consumer Protection law, to which New York law applies.

> FN5. Given that Plaintiff's decedent's prescription was prescribed and filled in New York, and she ingested it there, this Court asked counsel by letter dated March 2, 2006 to identify any possible conflict of law issues. The stipulation, which arose as a response to this letter, states that with regard to Counts I through IX, "the law of New York and the law of Pennsylvania are not in conflict, and thus, the laws of Pennsylvania should be applied thereto." Exhibit A, Joint Stip. of the Parties at p. 2.

IV. Contentions of the Parties

A. Defendants

Both Defendants GSK and Apotex contend Plaintiff's entire complaint must be dismissed, because (1) it is impliedly preempted by federal law, (2) Defendants

do not owe the Plaintiff a duty of care, (3) the learned intermediary doctrine applies, and (4) *Hahn v. Richter,* 543 Pa. 558, 673 A.2d 888, 891 (1996), precludes all Plaintiff's claims except those against the seller that sound in negligence.

Speaking to the threshold issue of preemption, Defendants urge that allowing Plaintiff's case to proceed would thwart the purpose of, and thus actually conflict with, the FDCA, and also that this Court must afford deference to the FDA's position that its regulations preempt state tort claims. Regarding a duty of care, GSK decrees that as an innovator drug manufacturer, it does not owe a legal duty to a consumer of the generic equivalent of its drug. Apotex asserts that pursuant to the statute governing FDA approval of generic drugs, it was not responsible for the form or content of the paroxetine hydrochloride labeling, and therefore it too did not owe a duty of care to Plaintiff. Third, Defendants urge that the learned intermediary doctrine applies to bar Plaintiff's complaint because adequacy is a question of law and the FDA's grant of original approval presumptively shows that the warnings were adequate. Finally, Defendants argue that *Hahn,* which held that "where the adequacy of warnings associated with prescription drugs is at issue, ... the manufacturer's negligence is the only recognized basis of liability," precludes all Plaintiff's claims except those that sound in negligence. 673 A.2d at 891.

Defendants also advance several arguments for dismissal with regards to Plaintiff's individual causes of action. First, Defendant Apotex contends that a claim for breach of implied warranty (Count II) is not

available in cases involving prescription drugs under Pennsylvania law. Next, Defendant GSK argues that Count III (fraud and violation of New York consumer protection statute), which is advanced only against it, fails because: (1) the fraud portion lacks the required particularity under F.R. Civ. P. 9(b), and (2) the consumer protection portion is alleged under the wrong statutory section, does not plead reliance, and is inconsistent with the learned intermediary doctrine. Third, both Defendants assert that Plaintiff's infliction of emotional distress counts (Counts V and VI) fail because the alleged wrongful conduct visited upon his wife did not occur in Plaintiff's presence. Next, Apotex urges Plaintiff's negligence claim (Count VII) must be dismissed because Plaintiff cannot show the existence of a duty and the negligence *per se* claim (Count VIII) is impliedly preempted. Last, as to the negligent misrepresentation claim (Count IX), Apotex urges that since it made no statements regarding the efficacy and safety of paroxetine hydrochloride to the FDA, Plaintiff cannot show the required element that Apotex knew or should have known that any such representations were false.

B. Plaintiff

Plaintiff argues that preemption is inappropriate for several reasons, including that: (1) the FDCA merely establishes minimum standards and permits manufacturers to unilaterally strengthen warning labels, and (2) deference is unsuitable because the FDA's policy has been inconsistent, and would violate the principle forbidding retroactive application of new rules. Next, Plaintiff urges that pursuant to Pennsylvania's nuanced duty of care analysis, the

Court should find that Defendant GSK owed him a duty of care. As to Apotex, Plaintiff asserts that Apotex, like all product manufacturers, cannot escape the duty it owes to its consumers. Further, Plaintiff contends that the learned intermediary doctrine requires an analysis of the adequacy of the warnings, which is a question of fact that cannot be determined at the 12(b)(6) stage. Finally, regarding *Hahn,* Plaintiff asserts that a broad reading is improper; *Hahn* is better understood to have a narrower holding.

As to the individual counts, Plaintiff argues his implied warranty claim is viable, attempting to distinguish the case cited by Apotex. He also cites to numerous specific allegations in his complaint supporting the fraud claim, and argues GSK's prolific, deceptive, "direct-to-consumer" advertising sufficiently supports his consumer protection claim. Next, Plaintiff contends that as to the infliction of emotion distress counts, it is sufficient that he observed the *result* of the alleged intentionally outrageous or negligent conduct. Advancing the same arguments as it did earlier, Plaintiff asserts he has shown a duty of care sufficient to underlie the negligence count, and that preemption is inapplicable to the negligence *per se* claim. Finally, Plaintiff maintains that at the 12(b)(6) stage, the Court must accept his averments that material submitted to the FDA and the labeling itself was intentionally false and misleading.

V. Federal Regulatory Process: Process to Obtain Approval from the FDA to Market and Sell Prescription Drugs

Analysis of the parties' arguments requires some understanding of the process for approval to market and sell generic drugs. The FDCA mandates that drugs are "safe and effective." 21 U.S.C. § 355(a). Therefore, pharmaceutical manufacturers must obtain regulatory approval for prescription drugs prior to marketing them. *Id.* For drugs that have not been marketed before, the process for approval requires submission of a new drug application ("NDA"). 21 U.S.C. § 355(a)-(i). The NDA must contain proof of the efficacy and safety of the drug, based on extensive laboratory testing. 21 U.S.C. § 355(b). Further, the FDCA requires refusal of any NDA that includes labeling that "is false or misleading in any particular." 21 U.S.C. § 355(d) (grounds for refusing new drug application). The obligation against misbranding drugs continues thereafter. 21 U.S.C. § 331(a), (b), (k). Under the FDCA, a drug is unlawfully misbranded when its labeling is false or misleading, or does not provide adequate directions for use or adequate warnings against any use dangerous to health. *Colacicco Amicus* at 4; 21 U.S.C. § 352.

Before 1984, generic drug manufacturers were required to submit their own NDA. *Foster v. American Home Products,* 29 F.3d 165 (4th Cir.1994) (applying Maryland law); *Tri-Bio Labs., Inc. v. United States,* 836 F.2d 135, 138-39 (3d Cir.1987). Because investigations conducted by the innovator companies were considered trade secrets, generic manufacturers were required to perform their own safety and effectiveness studies. This resulted in additional expenses being passed to consumers, and delay in bringing generic drugs to the market. *Id.*

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments ("H-W Amendments") to the FDCA, Pub.L. No. 98-417, 98 Stat. 1585 (codified at 21 U.S.C. § 355(j), 35 U.S.C. §§ 156, 271, 281), relaxed the procedure for obtaining approval from the FDA to market and sell a generic drug, allowing the generic maker to submit an abbreviated NDA ("ANDA"). *Id.*[FN6] The ANDA applicant need only certify that the generic manufacturer will produce a bio-equivalent of the brand name drug and that the labeling and warnings of the generic drug are identical to that of the approved innovator drug. 21 U.S.C. § 355(j)(2)(A).

> FN6. The purpose of the H-W Amendments is "to balance the interests of the generic drug manufacturers, who sought to avoid unnecessary testing, against the research investments of the innovator manufacturers, at the same time mindful of the public need for safe commercial drugs." *Tri-Bio Labs.*, 836 F.2d at 139.

After approval, a manufacturer may "add or strengthen a contraindication, warning, precaution, or adverse reaction" or "delete false, misleading, or unsupported indications for use or claims for effectiveness." 21 C.F.R. § 314.70(c)(6)(iii)(A), (D). However, in its *amicus* brief submitted to the Court in connection with this case, the FDA explained that "a generic drug manufacturer is not permitted to add a warning or caution to the label without prior approval from the FDA."*Colacicco Amicus* at 17. This is to assure that any changes to the label would not be "false or misleading," and thus misbrand the drug.

VI. Preemption Issues

In their briefs and at oral argument, both Defendants contended that Plaintiff's claims are preempted by the federal FDCA, urging that: (1) Plaintiff's claims are impliedly preempted under general preemption principles, and (2) the Supreme Court's holding in *Buckman Co. v. Plaintiffs' Legal Committee,* 531 U.S. 341, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2000) requires that we find preemption. Further, in response to this Court's request that the FDA file a brief on the novel preemption issues presented in this case, the government submitted an *amicus* brief to the Court on May 10, 2006 which also takes the position that Plaintiff's state law claims are barred by implied preemption.

A. Implied Preemption

Pursuant to the Supremacy Clause, any state law conflicting with the exercise of enumerated federal power is preempted. U.S. Const. art. VI, cl. 2. The United States Supreme Court has long recognized that federal preemption of state law can occur in three types of situations: (1) where Congress explicitly preempts state law ("express preemption"), (2) where preemption is implied because Congress has occupied the entire field ("field preemption"), and (3) where preemption is implied because there is an actual conflict between federal and state law ("conflict preemption"). *Schneidewind v. ANR Pipeline Co.,* 485 U.S. 293, 299-300, 108 S.Ct. 1145, 99 L.Ed.2d 316 (1988); *Pokorny v. Ford Motor Co.,* 902 F.2d 1116, 1121-22 (3d Cir.1990).

[1] Defendants concede that express and field preemption are not implicated, Def. Apotex's Mem. at 9, pursuing only the "conflict" preemption argument. Such a conflict exists where either (1) the state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress" or (2) it is "impossible for a ... party to comply with both state and federal law." *Geier v. Am. Honda Motor Co., Inc.*, 529 U.S. 861, 899, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000); *Pokorny*, 902 F.2d at 1120; *C.E.R.1988, Inc. v. Aetna Cas. & Sur. Co.*, 386 F.3d 263, 268 (3d Cir.2004).

Geier is the most recent in a consistent, long line of cases that articulate the Supreme Court's principles on implied preemption. In that case, an injured motorist and her parents brought a defective design claim against an automobile manufacturer based on a lack of an automobile airbag in their 1987 Honda Accord. *Geier*, 529 U.S. at 865, 120 S.Ct. 1913. After concluding that the National Traffic and Motor Vehicle Safety Act of 1966 did not expressly preempt petitioners' claims, the Court held that the claims nonetheless actually conflicted with the objectives of Federal Motor Vehicle Safety Standard 208 ("Standard 208") which gave automobile manufacturers a range of choices among different passive restraint devices which were to be gradually introduced over time. The Court reasoned that plaintiff's claims depended upon the manufacturer having a duty to install an airbag in all 1987 vehicles, which presented an obstacle to the variety and mix of devices that Standard 208 sought. *Id.* at 881, 120 S.Ct. 1913. Therefore, because the Supremacy Clause "forbids conflicts that make it impossible for private parties to comply with both state and federal

law," the Court concluded that plaintiff's claims were impliedly preempted. *Id.* at 873, 875, 886, 120 S.Ct. 1913.

Despite the generality of the definition of conflict preemption, the Supreme Court has urged caution in its application: "[B]ecause the States are independent sovereigns in our federal system, we have long presumed that Congress does not cavalierly preempt state-law causes of action." *C.E.R.1988,* 386 F.3d at 269-70 (quoting *Medtronic Inc. v. Lohr,* 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996) (case involving express preemption)). Thus, conflict preemption will be found only if the need for it is clear. *Pokorny,* 902 F.2d at 1122. In fact, "consideration under the Supremacy Clause starts with the basic assumption that Congress did not intend to displace state law." *Bldg. & Constr. Trades Council of Metro. Dist. v. Assoc. Builders & Contractors of Mass./R.I., Inc.,* 507 U.S. 218, 224, 113 S.Ct. 1190, 122 L.Ed.2d 565 (1993).

In contending that Plaintiff's claims are impliedly preempted by federal law, Defendants principally assert that assigning state tort liability would thwart the purpose of-and thus actually conflict with-the Hatch-Waxman Amendments.[FN7] Further, Defendants argue that under clearly established caselaw, this Court must afford deference to the FDA's position that its regulations preempt state tort claims for inadequate warnings, which it has articulated in several *amicus* briefs and in the preamble to new drug labeling regulations issued in 2006. *See*Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed.Reg. 3922-97 (Jan. 24, 2006)

(effective date June 30, 2006) (to be codified at 21 C.F.R. pts. 201, 314, 601) (hereinafter, "Preemption Preamble" to the "Final Rule") (Def. Apotex Mem. at 9-15; Def. GSK Mem. at 9; Apotex Supp. Mem. at 18-24; GSK Supp. at 10-18; Apotex 2nd Supp. Mem. at 2-10; GSK 2nd Supp. Mem. 1-5).

> FN7. See *supra* Part V for an in depth discussion of the Hatch-Waxman Amendments.

In its *amicus* brief to this Court, the FDA goes even further, asserting that because prior to October 2003, the agency had repeatedly determined that there was inadequate evidence of an association between adult use of SSRIs and suicidality, Plaintiffs' state law failure-to-warn claims are preempted because such a warning statement would actually have been "false and misleading," and thus contrary to federal law. *Colacicco Amicus*, at 1. We address these arguments in turn.

1. Deference to the FDA's Position that Plaintiff's Claims are Preempted

The Defendants and the FDA point to several pieces of evidence which reflect the FDA's position that Plaintiff's inadequate warning claims are preempted: (1) the May 10, 2006 *amicus* brief filed in this case representing that the FDA would consider such a warning false and misleading (as well as two prior *amicus* briefs filed in other cases by the FDA in 2005 and 2002, respectively, indicating the same), (2) the 2006 Preemption Preamble, an official agency statement purporting to establish preemption of conflicting state law claims.

[2] The FDA's view is critical to this Court's analysis because Supreme Court precedent dictates that an agency's interpretation of the statute and regulations it administers is entitled to deference. *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 844, 104 S.Ct. 2778, 81 L.Ed.2d 694 (1984) (holding that it has been "long recognized that considerable weight should be accorded to an executive department's construction of a statutory scheme it is entrusted to administer"). *See also Thomas Jefferson Univ. Hosp. v. Shalala*, 512 U.S. 504, 512, 114 S.Ct. 2381, 129 L.Ed.2d 405 (1994); *NVE Inc. v. Dept. of Health & Human Servs.*, 436 F.3d 182, 186 (3d Cir.2006); *C.E.R.1988*, 386 F.3d at 271 n. 11.However, deference is not absolute; in deciding whether to afford it, courts should review *inter alia* the consistency with which the agency has applied the particular interpretation. *NLRB v. N.J. Bell Tel. Co.*, 936 F.2d 144, 147 (3d Cir.1991) (citing *West v. Bowen*, 879 F.2d 1122, 1134 (3d Cir.1989)).

In the context of preemption specifically, the Supreme Court held in 1985 that in the absence of clearly expressed Congressional intent or subsequent developments that reveal a change in that position, the FDA's position on the preemptive scope of its regulatory authority "is dispositive." *Hillsborough County v. Automated Med. Labs. Inc.*, 471 U.S. 707, 714, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985).

[3] Further, the Court has made clear that such preemptive intent may properly be communicated in *amicus* briefs, *Geier*, 529 U.S. at 883, 120 S.Ct. 1913, as well as in "regulations, preambles, interpretive statements and responses to comments." *Hillsborough County*, 471 U.S. at 718, 105 S.Ct. 2371.

In recent years, each time the Supreme Court has confronted the question of whether the FDCA preempts state law, it has deferred to the FDA's preemption position.[FN8] *See Geier*, 529 U.S. at 883, 120 S.Ct. 1913 (noting that the Court "place[s] some weight upon [the federal agency's interpretation of the regulation's] objectives and its conclusion ... that a tort suit ... would stand as an obstacle to the accomplishment and execution of those objectives"); *Medtronic*, 518 U.S. at 496, 116 S.Ct. 2240 (holding that state law claims involving FDCA section 510(k) medical devices, which are subjected to a relatively cursory approval process, were not preempted because the FDA had taken the position that its regulations only preempted claims involving section 360e(c) devises, which go through a rigorous pre-market approval process); *Buckman*, 531 U.S. at 353, 121 S.Ct. 1012 (in which the Court's holding that the FDCA, as amended by the Medical Devices Amendment ("MDA"), impliedly preempted patients' state law "fraud-on-the-agency" claims mirrored the position taken by the FDA in its *amicus* brief submitted to the court [FN9]).

> FN8. For a history of how the Supreme Court has responded to the FDA's position on preemption, *see* Eric G. Lasker, *How Will FDA's New Label Rule Impact Drug Litigation?*, 9 No. 10 Andrews Drug Recall Litig. Rep. 9, at 2 (Mar. 13, 2006).
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> FN9. *See* Brief for United States as *Amicus Curiae*, *Buckman Co. v. Plaintiffs' Legal Comm.*, Civ. No. 98-1768, 531 U.S. 341, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001) (available at 2001 WL 167647).

[4] The Third Circuit has not rendered an opinion as to the level of deference that should be afforded to the FDA's position on whether the FDCA impliedly

preempts state failure-to-warn claims. However, the Third Circuit considered whether to defer to the FDA's position on express preemption in the 2004 case *Horn v. Thoratec Corp.*, 376 F.3d 163, 171 (3d Cir.2004). *Horn* held that the plaintiff's state law claims against a heart valve manufacturer were preempted by the express preemption provision of the MDA. *Id.* at 180. In coming to this conclusion, the court stated that the Supreme Court's decision in *Medtronic* required it to afford deference to the FDA's position that the claims were preempted. *Id.* at 179. Moreover, it held that this was the case even though this stance was a change from the FDA's prior position. *Id.* (noting "we cannot agree [with Plaintiff] that the FDA's position is entitled to no deference or 'near indifference' simply because it represents a departure from its prior position."). The court noted that the Supreme Court in *Chevron* held that a "revised interpretation by an agency is [still] entitled to deference because an initial agency interpretation is not instantly carved in stone,"*Id.*(citing *Chevron*, 467 U.S. at 863-64, 104 S.Ct. 2778), and that an agency may change its position "so long as it can justify its change with reasoned analysis." *Id.* (citing *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42, 103 S.Ct. 2856, 77 L.Ed.2d 443 (1983)). *Horn* held that it was "fully persuaded" that the FDA adequately justified its change in position on preemption. *Id.* Importantly, while the facts of *Horn* involved the express preemption provision of the MDA, to which there is no corollary part in the prescription labeling provisions of the FDCA, the *Horn* court broadly announced a policy of affording deference to the FDA's position on preemption, and did not narrow the holding only to cases involving express preemption.

a The Government's Amicus Briefs

In the *amicus* brief submitted to this Court, the FDA re-affirmed its view that Plaintiff's claims are preempted. *Colacicco Amicus* at 1, 13, 15. Explaining this position, the FDA noted that the FDCA prohibits the misbranding of drugs. 21 U.S.C. § 331(a), (b), (k). As explained above, under the FDCA, a drug is unlawfully misbranded when its labeling is false or misleading, or does not provide adequate directions for use or adequate warnings against any use dangerous to health. *Colacicco Amicus* at 4. Therefore, to the extent that before and up to October 2003,[FN10] the date of Plaintiff's decedent's death, the FDA specifically and repeatedly rejected claims that adult use of SSRI's was associated with increased suicidality because there was no reasonable evidence to support the linkage, the FDA contends that any such warning would have been false or misleading, and contrary to the public interest. For this reason, the FDA asserts that Plaintiff Colacicco's failure-to-warn claims are preempted by federal law. *Id.* at 17.

FN10. The brief, accompanied by a lengthy appendix, outlines how on no less than six occasions between July 1991 and October 2003, the FDA rejected proposals seeking changes in drug labeling regarding suicide for SSRIs. In briefs responding to the *Colacicco Amicus*, Defendants argued that the Court may consider this information without converting the 12(b)(6) into a motion for summary judgment. (Def. Apotex 4th Supp. Mem at 3-8; Def. GSK 4th Supp. Mem at 5-8). Although the information about the FDA rejecting proposals seeking changes in drug labeling is evidence outside the record, a court may properly take judicial notice of public records and consider them in a 12(b)(6) motion. *Pension Benefit Guaranty Corp. v. White Consol. Indus. Inc.*, 998 F.2d 1192, 1197 (3d Cir 1993). However, *how* the FDA came to

> its conclusion is far less relevant than the fact that the FDA *did* conclude Plaintiff's claims are preempted. It is the latter to which we give deference, and therefore these extra-record factual allegations are not determinative to our conclusion.

Moreover, the FDA explained that public policy requires that warnings be scientifically substantiated. Dissemination of unsupported warnings, the FDA urged, would deprive patients of efficacious treatment, thereby chilling the drug's otherwise beneficial use. *Id.* at 13. The FDA also flatly rejected the often-cited proposition by many courts refusing to apply preemption in prescription drug cases that 21 C.F.R. § 314.70(c) permits drug makers to unilaterally strengthen a warning label without FDA approval. *Id.* at 6, 17. Instead, it decreed that despite what numerous lower courts [FN11] around the nation have stated, a "*drug manufacturer is not permitted to add a warning or caution to the label without prior approval from the FDA.*" *Id.* at 17 (emphasis added).

> FN11. *See, e.g., McNellis v. Pfizer, Inc.*, Civ. No. 05-1286, 14 (D.N.J. Dec. 29, 2005); *Witczak v. Pfizer*, 377 F.Supp.2d 726, 729 (D.Minn.2005); *Zikis v. Pfizer, Inc.*, Civ. No. 04-8104, 6 (N.D.Ill. May 9, 2005); *Cartwright v. Pfizer*, 369 F.Supp.2d 876, 882 (E.D.Tex.2005). These case are discussed below at pages 32-34. However, neither the Supreme Court nor the Third Circuit has spoken on this issue.

This position is consistent with the view taken in two prior *amicus* briefs prepared by the FDA in other failure-to-warn cases. *See* Brief for United States as *Amicus Curiae* Supporting Defendant, *Kallas v. Pfizer, Inc.*, Civ. No. 2:04-cv-0998, 34, 37-38 (D.Utah Sept. 15, 2005) (FDA amicus brief arguing that

plaintiff's failure-to-warn claims were preempted because the FDA lacked reasonable evidence of an association between SSRIs and suicidality in children in November 2002; thus, the proposed warning would have misbranded Zoloft, the SSRI at issue) ("*Kallas Amicus* "); Brief for United States as *Amicus Curiae* Supporting Defendant, *Motus v. Pfizer, Inc.*, Civ. Nos. 02-cv-55372, 02-cv-55498, (9th Cir. Sept.10, 2002), 2002 WL 32303084, at *16 (amicus brief submitted by FDA contending plaintiff's failure-to-warn case was preempted because, before plaintiff's decedent's death in 1998, the FDA had considered, and rejected, claims that SSRIs were linked to suicidal behavior in adults, and any warning label would have been "false or misleading" and would therefore have misbranded Zoloft, the SSRI at issue) ("*Motus Amicus* ").[FN12] *See also* Lori J. Parker, *Proof of Injury Resulting from Antidepressant Medication*, 87 Am.Jur. Proof of Facts 3d 119, § 3 (2006).

> FN12. Notably, while the FDA filed *amicus* briefs in both cases, neither *Kallas* nor *Motus* resulted in a judicial decision as to preemption. The *Kallas* case settled before the District of Utah rendered a decision. *Kallas v. Pfizer, Inc.*, Civ. No. 2:04-cv-0998 (D.Utah Oct. 24, 2005) (order granting stipulated motion to dismiss pursuant to settlement). In *Motus*, while the Ninth Circuit rendered a decision affirming summary judgment in favor of defendant, it did so based on lack of causation, declining to reach the issue of preemption. *Motus v. Pfizer, Inc.*, 358 F.3d 659, 660 (9th Cir.2004) (because plaintiff failed to establish a sufficient causal link between her husband's suicide and the drug manufacturer's conduct, "we need not reach the preemption issues raised by [defendant]").

According to the FDA, therefore, it is clear that any insert in October 2003 associating use of paroxetine hydrochloride with suicidality would have constituted

misbranding, because it was contrary to the scientific evidence, and thus "false and misleading." Pursuant to the principles announced in the Supreme Court's decisions in *Chevron, Medtronic,Geier* and their progeny, as well as the Third Circuit's broad holding in *Horn,* it is therefore appropriate to afford deference to the FDA's position based on the *Colacicco Amicus* alone.

However, in his response to the *Colacicco Amicus,* Plaintiff argues that we ought not pay the *amicus* any deference because (1) the FDA glosses over the importance of 21 C.F.R. § 314.70, which it argues allows manufacturers to strengthen labels without prior FDA approval-and which almost every court that has heretofore rejected preemption has cited, and (2) the FDA has no authority to simply declare that a drug is misbranded, and, at any rate, such opinion is merely hypothetical, as at no time prior to Plaintiff's decedent's death did either Defendant request a stronger warning. (Pl.'s 4th Supp. Mem. at 3 n. 3, 5, 8-10).

We disagree. As to the Plaintiff's first objection, Plaintiff notes that the plain language of § 314.70 states that the holder of an approved application may make changes in the labeling to "add or strengthen a contraindication, warning, precaution, or adverse reaction," and may "*commence distribution of the drug product involved upon receipt by the agency* of a supplement for the change."21 C.F.R. § 314.70(c)(6)(iii)(A). He thus contends the provision's plain language explicitly permits manufacturers to strengthen labels *without* prior FDA approval. (Pl.'s 4th Supp. Mem. at 3 n. 3). However, 21 C.F.R. § 314.150, cited by the FDA in its *amicus* brief and by

Defendant Apotex, directly supports the FDA's position that generic drug makers *can not* unilaterally strengthen their drug. 21 C.F.R. § 314.150 states that the FDA will withdraw approval of a generic maker's ANDA if the label ceases to be identical to that of the name-brand drug. Interpreting § 314.150, the FDA explained, "[i]f an ANDA applicant believes new safety information should be added to a product's labeling, it should contact FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised. After approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised." 57 Fed.Reg. at 17961. Moreover, despite the plain language of § 314.70, and even if the FDA's position were not bolstered by 21 C.F.R. § 314.150, this Court believes that principles of deference do not allow us to question the FDA's interpretation of its own regulations-e.g. that generic drug manufacturers can not make changes without prior approval.

As to the second assertion, Plaintiff argues that the FDA must prosecute an enforcement action to establish a drug is misbranded, citing 21 U.S.C. §§ 331-37, 352. However, these sections merely discuss the requirements of an enforcement or injunctive action if one is brought; no where does the statute declare that the FDA must bring a prosecution to state an *opinion* as to whether a particular drug would have been misbranded if a certain warning had been attached. Further, it is not in dispute that the FDA's position is a hypothetical. In fact, it is in part *because* neither Defendant requested a stronger

warning that the vacuum of information was created that necessitated this Court asking the FDA to render an opinion as to preemption. Moreover, we note that the Supreme Court has explicitly stated that *amicus* briefs are an appropriate form to express preemptive intent, *Geier*, 529 U.S. at 883, 120 S.Ct. 1913, which, pursuant to *Chevron*,*Medtronic*,*Geier*, we must afford significant deference.[FN13]

> FN13. Plaintiff also argues *Sprietsma v. Mercury Marine*, 537 U.S. 51, 123 S.Ct. 518, 154 L.Ed.2d 466 (2002) requires that this Court reject the FDA's position. In *Sprietsma*, the Supreme Court held the Federal Boat Safety Act (FBSA) did not impliedly preempt plaintiff's common law tort claims, arising out of the defendant manufacturer's failure to install propeller guards on a boat engine. *Id.* at 64-68, 123 S.Ct. 518. This case, however, is easily distinguishable. First, in *Sprietsma*, the Coast Guard *declined* to regulate boat propellers completely; they decided to "take no regulatory action." *Id.* at 65, 123 S.Ct. 518. Here, the FDA's mandate is to affirmatively regulate the approval and labeling of prescription drugs. Second, *Sprietsma* in part depended on the fact that states were free to adopt their own regulation to regulate propellers. This of course is not so with prescription labeling under the FDCA, where any state law effort to brand a drug different from that approved by the FDA would result in misbranding. Finally, *Sprietsma* discusses-and distinguishes-*Geier*, noting that the Coast Guard stated it did *not* view its regulatory actions as having preemptive effect, in obvious contrast to our facts. In sum, *Sprietsma* is inapposite to the case at hand.

b. The Preemption Preamble

However, we need not base our conclusion on the *amicus* briefs alone. In early 2006, the FDA additionally promulgated what we refer to as the "Preemption Preamble," which states that, "whether

it be in the old or new format, [the FDCA] preempts conflicting or contrary state law," and "conflicting" includes state failure-to-warn claims. 71 Fed.Reg. at 3934, 3936. As in its *Colacicco Amicus* brief, the FDA in the Preemption Preamble specifically rejected the two main arguments advanced by those courts rejecting preemption: (1) that the FDCA imposes only minimum standards for labeling, and (2) drug manufacturers have the ability to strengthen warnings without FDA approval. 71 Fed.Reg. at 3934-35; *see also* Eric G. Lasker, *How Will FDA's New Label Rule Impact Drug Litigation?*, 9 No. 10 Andrews Drug Recall Litig. Rep. 9, at 2 (Mar. 13, 2006). As to the "misunderstanding" that FDA labeling requirements represent a minimum safety standard, the FDA Preemption Preamble interprets the FDCA to "establish both a 'floor' and a 'ceiling.' " *Id.* Regarding the argument that manufacturers can modify labels without FDA approval, the FDA urges that "in practice, manufacturers typically consult with FDA before doing so to avoid implementing labeling changes with which the agency ultimately might disagree." *Id.* Also, as in the *Colacicco Amicus* brief, the Preamble asserts that "state-law attempts to impose additional warnings can lead to labeling that does not accurately portray a product's risks, thereby potentially discouraging safe and effective use of approved products." *Id.*

As discussed above, it is abundantly clear that the FDA's position is entitled to significant deference. *Geier*, 529 U.S. at 883, 120 S.Ct. 1913; *Chevron*, 467 U.S. at 844, 104 S.Ct. 2778; *Hillsborough County*, 471 U.S. at 714, 105 S.Ct. 2371; *Horn*, 376 F.3d at 180. However, notwithstanding the unambiguous position taken by the FDA in the *Colacicco Amicus*

and in the Preemption Preamble, and despite the general rule requiring deference, Plaintiff argues that deference is not appropriate in this case for three reasons: (1) the preamble is mere legal argument that deserves no weight, (2) the FDA's policy has been inconsistent, and (3) it would be improper to retroactively apply the Preamble.

Weight Afforded to FDA's Position

First, Plaintiff argues that the Preemption Preamble amounts to mere legal argument that should not affect this court's inquiry. (Pl.'s Supp. Mem. at 7-11). We disagree. In this case, "the subject matter [of the FDCA] is technical; and the relevant history and background are complex and extensive," and we find that the FDA is "uniquely qualified to comprehend the likely impact of state requirements." *Geier,* 529 U.S. at 883, 120 S.Ct. 1913, citing *Medtronic,* 518 U.S. at 496, 116 S.Ct. 2240. Given the overwhelming caselaw on the issue of deference, and specifically the Supreme Court's holdings in *Geier* and *Hillsborough County* that preemptive intent may properly be communicated in *amicus* briefs, preambles and interpretive statements, we find Plaintiff's argument lacks merit. *Geier,* 529 U.S. at 883, 120 S.Ct. 1913; *Hillsborough County,* 471 U.S. at 718, 105 S.Ct. 2371.Further, it is not the function of this Court, or for a jury empaneled to decide this case, to substitute its judgment for the FDA's about these medical issues. Congress has given the FDA broad power, the President has appointed its executives, some subject to the advice and consent of the Senate, and it has rendered its judgment on these issues. The FDA has acted within its authority, and this Court must respect its expert judgment that an October 2003

warning label other than approved by the FDA would have been in direct, actual conflict with federal law.

d. Inconsistency of the FDA's Position

Second, Plaintiff argues that despite the FDA's statements that the Preemption Preamble "represents the government's long standing views" on preemption, 71 Fed.Reg. at 3934, and that its argument in the *Colacicco Amicus* that its position on "federal preemption of ... failure-to-warn claims [does not] constitute a wholesale change in agency position," in fact, the FDA has not been consistent in its position on preemption. Plaintiff points to two past statements made by the FDA demonstrating that it did *not* always consider its regulations to have preemptive effect. *See*65 Fed.Reg. 81082, 81103 (Dec. 22, 2000) (FDA taking stance in initial proposed version of preamble to what was ultimately enacted as the Final Rule that its regulations are minimum standards, and *do not preempt state tort claims*); 63 Fed.Reg. 66378, 66384 (Dec. 1, 1998) ("[F]ederal preemption could unduly interfere with the goals and objectives of existing State programs ... This final rule is intended to complement these State efforts, not replace or hinder them."). (Pl.'s Supp. Mem. at 7-11).

In its response to the *amicus* brief, GSK offered some compelling reasons why the 1998 statement ought not be considered inconsistent with the FDA's current position. GSK points out that the 1998 declaration related to the FDA's final regulation on Patient Medication Guides, which is information provided directly to patients, usually by pharmacists. Drug stores and pharmacies, in turn, have traditionally been regulated by the States, not the FDA. *See*,

e.g.,49 Pa.Code § 27.19 (State Board of Pharmacy's regulation concerning prospective drug review and patient counseling). Thus, to the extent that the FDA commented that federal preemption could unduly interfere with state programs, it appears this concerned state programs regarding what information pharmacists must provide *directly to patients.* Because the protections afforded by some of these state programs exceeded that required by federal law, the FDA commented that it did not intend to displace these programs. 63 Fed.Reg. at 66384. Accordingly, we concur with GSK that the 1998 statement does not undermine the FDA's current position on preemption, which concerns what information must be provided *to physicians* about prescription drugs, the regulation of which unquestioningly is exclusively a federal function.

The inconsistency in the December 2000 declaration is more problematic. We find it is difficult to reconcile the FDA's current position with that statement, which was made in the FDA's initial notice of its intent to revise the prescription drug labeling regulations, which ultimately was enacted as the Final Rule. At that time, the FDA "determined that this proposed rule *does not contain policies that have federalism implications or that preempt State law.*" 65 Fed.Reg. at 81103 (emphasis added). Further, despite our specifically asking the FDA to address whether their current position can be reconciled with the December 2000 statement, the *Colacicco Amicus* brief is completely silent on the 2000 statement. *See* Letter to Counsel for the Government Re: Follow-Up Questions for the Amicus Brief, *Colacicco v. Apotex*, Civ No. 05-5500 (Doc. No. 44) (E.D.Pa. May 4, 2006); *Colacicco Amicus* at 20.[FN14] Nonetheless, although

consistency of an administrative agency's position is a factor, as *Chevron* made clear, there is no longer any justification for not giving deference to an agency's interpretation of law merely because it is not the agency's longstanding position. *Chevron*, 467 U.S. at 863-64, 104 S.Ct. 2778 (holding "[t]he fact that the agency has from time to time changed its interpretation ... does not ... lead us to conclude that no deference should be accorded the agency's interpretation of the statute. An initial agency interpretation is not instantly carved in stone." *See also Horn*, 376 F.3d at 179 ("[W]e cannot agree [with Plaintiff] that the FDA's position is entitled to no deference ... simply because it represents a departure from its prior position.")).[FN15] "On the contrary, the agency, to engage in informed rulemaking, must consider varying interpretations and the wisdom of its policy on a continuing basis." *Chevron*, 467 U.S. at 863-64, 104 S.Ct. 2778; *see also* Antonin Scalia, *Judicial Deference to Administrative Interpretations of Law*, 1989 Duke L.J. 511, 518 (1989)(*Chevron* embraces concept that merely because agency interpretation is "new" or "changing," it is not somehow suspect).

FN14. In their brief responding to the *Colacicco Amicus*, Defendant GSK tries to argue that the 2000 statement is not inconsistent, because it was made pursuant to Exec. Order No. 13132, 64 Fed.Reg. 43255 (Aug. 4, 1999), which itself does not mention tort liability. Order 13132, GSK asserts, merely requires agencies to state whether its policies have "federalism implications," defined as federal actions that "have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government." 65 Fed.Reg. at 81103. GSK therefore contends that because the definition does not mention private tort suits, it was proper for the FDA to find there

were no "federalism implications" of its proposed rule. GSK's argument misses the mark. Certainly to the extent that the FDCA labeling regulations preempt state tort law, this would have "federalism implications," in that a policy stating that federal law completely trumps state failure-to-warn claims axiomatically has a "substantial [effect] ... on the relationship between the national government and the States."

FN15. As discussed *supra*, we recognize that *Horn* dealt with *express* preemption under the Medical Device Amendments ("MDA") to the FDCA, which unlike the prescription drug labeling portions of the FDCA, contained an express preemption provision. However, as the Third Circuit's holdings were broadly stated, we do not believe this affects the amount of deference a district court must afford the FDA's position on preemption.

Moreover, we do find it significant that after 2000, the FDA has been very consistent. [FN16] On four occasions-in the *Colacicco Amicus,* the *Preemption Preamble,* the *Kallas Amicus,* and the *Motus Amicus*-it set forth detailed analyses of its position that the Supremacy Clause bars state tort liability specifically for failure to include a warning on a drug label that is in conflict with or contrary to the warnings approved by the FDA. *See Colacicco Amicus, Preemption Preamble, Kallas Amicus, Motus Amicus.* Moreover, the 1998 and 2000 statements in the Federal Register referred more generally to the regulations and not to the specific circumstances here-where Plaintiff's proposed warning would have misbranded the drug. *Dusek v. Pfizer, Inc.,* No. Civ.A. H-02-3559, 2004 WL 2191804, *6 (S.D.Tex. Feb.20, 2004) (holding state failure-to-warn claims were preempted, because any warning label linking said drugs to suicide would have been false and misleading). Accordingly, even though the FDA's prior position on preemption has not been entirely consistent, this Court finds it proper

to give significant weight to the FDA's unambiguous statement in the *Colacicco Amicus* brief and in the Preemption Preamble that Plaintiff's claims are preempted. *Hillsborough County,* 471 U.S. at 714, 105 S.Ct. 2371; *Chevron,* 467 U.S. at 844, 104 S.Ct. 2778; *Horn,* 376 F.3d at 179.*See also Needleman v. Pfizer, Inc.*, 03-CV-3074, 2004 WL 1773697, *2-5 (N.D.Tex. Aug.6, 2004); *Dusek,* 2004 WL 2191804 at *10. Accordingly, based on deference alone, this Court would deem any state failure-to-warn claim impliedly preempted.

> FN16. Further, we find it irrelevant whether the FDA's change in position since 2000 has been because of medical judgments, change in governance, or something else.

e. Retroactivity of the Preamble

Finally, Plaintiff questions whether the Preemption Preamble, promulgated in 2006, may be retroactively applied to the October 2003 death of the decedent in this case. This appears to be an issue of first impression, as only two courts have had occasion to mention the Final Rule, and neither have specifically considered the question of retroactivity as to the Preemption Preamble in particular. *Abramowitz v. Cephalon, Inc.*, 2006 WL 560639, *5 (N.J.Super.Mar. 3, 2006); *Laisure-Radke v. Par Pharm.*, Civ. No. 03-3654, 2006 WL 901657, *3 (W.D.Wash. Mar.29, 2006).

A brief primer on administrative law is necessary to address the parties' claims because the law governing administrative rule-making, and in turn retroactivity, largely hinges on how the agency's stance is classified-that is, whether the agency's position is a substantive rule, an adjudicative rule, an interpretive

rule, or a statement of policy under the Administrative Procedure Act ("APA").

[5] The APA defines a "substantive" or "legislative" rule as "an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency"5 U.S.C. § 551(4). These rules have the force and effect of law and must be promulgated in accordance with the proper notice and comment procedures under the APA.*Beazer E., Inc. v. U.S. Envtl. Prot. Agency, Region III,* 963 F.2d 603, 606 (3d Cir.1992). "Interpretive" rules, on the other hand, seek only to interpret the meaning already in properly issued regulations and are meant "to give guidance to its staff and affected parties as to how the agency intends to administer a statute or regulation." *Id.; Daughters of Miriam Ctr. for the Aged v. Mathews,* 590 F.2d 1250, 1258 (3d Cir.1978). Thus, "if the rule in question merely clarifies or explains existing law or regulations, it will be deemed interpretive." *Bailey v. Sullivan,* 885 F.2d 52, 62 (3d Cir.1989). Further, interpretive rules and statements of policy are exempted from the APA's notice and comment requirement. *Beazer,* 963 F.2d at 606.

[6] Similarly excluded from the APA's notice and comment requirements, and lacking the force of law, are "general statements of policy." *United States v. Mead Corp.,* 533 U.S. 218, 121 S.Ct. 2164, 2173-75, 150 L.Ed.2d 292 (2001); *Madison v. Res. for Human Dev., Inc.,* 233 F.3d 175, 179 (3d Cir.2000). Although the term is not defined in the APA, the Supreme Court has afforded deference to the definition proffered in the Attorney General's 1947 Manual on

the Administrative Procedure Act ("Attorney General's Manual"), stating it is a pronouncement "issued by an agency to advise the public prospectively of the manner in which the agency proposes to exercise a discretionary power." *Lincoln v. Vigil,* 508 U.S. 182, 197, 113 S.Ct. 2024, 124 L.Ed.2d 101 (1993); Attorney General's Manual 30, n. 3 (1947).

The Supreme Court has made clear that substantive rules may not be retroactively applied. *Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 208, 109 S.Ct. 468, 102 L.Ed.2d 493 (1988).[FN17] Here, while the rule to which the Preemption Preamble is attached is the type of rule governed by *Georgetown University,* the preamble lacks force of law, and is not a substantive rule. However, it is not initially clear whether the Preemption Preamble is an "interpretive rule" or a "statement of policy."

> FN17. Equally clear is the retroactivity of pronouncements announced by adjudication, where an administrative agency issues a regulation through an adversary proceeding, based on the facts and the parties before it. Unlike the case of substantive rule-making, the outcome in adjudication is often-and permissibly-applied retroactively to the parties in the case at hand, so long as this will not result in "manifest injustice." *Bowen*, 488 U.S. at 219-20, 109 S.Ct. 468 (Scalia, J., concurring). However, as the FDA's preemption policy was not announced via adjudication in the instant case, the retroactivity rules for adjudications are inapplicable.

In *Appalachian States Low-Level Radioactive Waste Commission v. O'Leary,* 93 F.3d 103, 113 (3d Cir.1996), the Third Circuit held that because an interpretive rule merely clarifies what existing rights and obligations had always been, retroactivity

concerns are irrelevant. *Accord: United States v. Tomasino*, 206 F.3d 739 (7th Cir.2000); *Cowen v. Bank United of Tex., FSB*, 70 F.3d 937, 943 (7th Cir.1995); *Pope v. Shalala*, 998 F.2d 473, 483 (7th Cir.1993); *Ill. by the Ill. Dep't of Pub. Aid v. Bowen*, 786 F.2d 288, 292 (7th Cir.1986). *Cf. Beazer*, 963 F.2d at 609 (in case involving the retroactive application of the EPA's interpretation of certain regulatory language via adjudication, which the Third Circuit held to be proper, stating in *dicta* that the "[APA] ... expressly prohibit[s] an agency from retroactively imposing an interpretive rule upon a regulated party").

However, if the Preemption Preamble is a statement of policy, the law on retroactivity is less clear, particularly in the Third Circuit. While most circuits adhere to the definition of policy statements as pronouncements to "advise the public *prospectively*," *Mada-Luna v. Fitzpatrick*, 813 F.2d 1006, 1014 (9th Cir.1987); *Am. Hosp. Ass'n v. Bowen*, 834 F.2d 1037, 1046 (D.C.Cir.1987); *Burroughs Wellcome Co. v. Schweiker*, 649 F.2d 221, 224 (4th Cir.1981); *Am. Bus. Ass'n v. United States*, 627 F.2d 525, 529 (D.C.Cir.1980), the Eleventh Circuit has explicitly held that a statement of policy that clarifies existing law may be applied retroactively. *Jean v. Nelson*, 711 F.2d 1455, 1479 (11th Cir.1983) . While the Third Circuit has not addressed this issue, we conclude that it would follow the definition in the Attorney General's Manual, which has been afforded deference by the Supreme Court and which states that policy statements only apply *prospectively*, as well as the strong weight of authority that favors the view that policy statements may not be applied retroactively.

Lincoln, 508 U.S. at 197, 113 S.Ct. 2024; Attorney General's Manual 30, n. 3.

Thus, having determined that in the Third Circuit, an "interpretive rule" likely may apply retroactively, but a "statement of policy" likely may not, our determination as to which category the Preemption Preamble falls into is important. Certainly to say that the law in this area is less than clear is an understatement. *See Cmty. Nutrition Inst. v. Young*, 818 F.2d 943, 946 (D.C.Cir.1987) (quoting authorities describing the distinction between legislative rules and general policy statements as "tenuous," "blurred," "baffling," and "enshrouded in considerable smog"). *See also Am. Bus. Ass'n*, 627 F.2d at 529 (distinction between categories of agency pronouncements is actually "enshrouded in considerable smog...."); *Noel v. Chapman*, 508 F.2d 1023, 1030 (2d Cir.1975). In fact, we can not actually envision a reason for the outcome regarding retroactivity to differ based on whether a particular communication is a policy statement or an interpretive rule, as both are agency interpretations of regulatory schemes. Thus, to the extent we must make this choice based on the confused caselaw in this area, it seems to put form before substance.

That said, the FDA's position that it is merely clarifying its "longstanding views on preemption," 71 Fed.Reg. at 3934-e.g., that it is only "only remind[ing the] affected parties of existing duties"-weighs heavily in favor of concluding that the Preemption Preamble is an interpretive rule. *Beazer*, 963 F.2d at 606. This is because, while not dispositive, the promulgating's agency's view "that a new statement is a clarification of existing law ... is generally given much weight."

Heimmermann v. First Union Mortgage Corp., 305 F.3d 1257, 1260 (11th Cir.2002). Accordingly, we find that the Preemption Preamble merely clarifies existing law and has no prohibited retroactive effect.[FN18] However, we also conclude that the issue of retroactivity is not dispositive, because the Preemption Preamble is only one of several pieces of evidence which reflect the FDA's position that Plaintiff's claims are preempted. Thus, even if the Preamble is not retroactive, we would still come to the same conclusion affording deference based on the FDA's opinion as expressed in its current and prior *amicus* briefs.

FN18. Plaintiff argues that even if the court decides it may be retroactively applied, the Preemption Preamble-published on January 24, 2006 and connected to a substantive rule due to take effect June 30, 2006-cannot be applied because the rule is not yet in effect. (Pl's 2nd Supp. Mem. at 6-7). Defendants assert that the Preemption Preamble, unlike the substantive rule amendments to which is it attached, is an advisory opinion that cannot be understood to go "into effect." (Def. GSK's 2nd Supp. Mem. at 3; Def. Apotex's 2nd Supp. Mem. at 10-11). Neither party provided citations, and this Court's review of caselaw in and outside of the Third Circuit did not uncover anything on point. However, using principles of administrative law as our guide, we note that neither a policy statement nor an interpretive rule has the force of law. Similarly, under the FDA's own regulations, a preamble to a rule is an "advisory opinion," that is "*not ... a legal requirement.*" 21 C.F.R. § 10.85(j) (emphasis added). Because by all accounts the preamble lacks the force and effect of law, we agree with Defendants that an effective date analysis would accordingly be irrelevant. The Preamble should be given deference as of the date it was published, January 26, 2006.

2. Other Evidence Supporting Implied Preemption

As additional evidence of conflict preemption, Apotex argues that tort liability for inadequate warnings would "stand[ ] as an obstacle to the accomplishment and execution of the full purposes and objectives" of the FDCA.*Geier*, 529 U.S. at 899, 120 S.Ct. 1913. First, Apotex contends that to impute liability for failing to change the label when, as part of the approval process under the ANDA, it was *required* to use verbatim the language of Defendant GSK's warning label, inherently conflicts with the FDCA. Further, Apotex urges that imposing a duty to develop or strengthen warning labels would essentially constitute a return to the drug approval scheme in place before the H-W Amendments, thus conflicting with the Act's statutory purpose to relax the generic approval process. Finally, Apotex points to numerous cases outside the Third Circuit, which has not addressed the issue, holding that the FDCA preempts state tort claims for injuries resulting from ingestion of a prescription drug. *See, e.g., Needleman*, 2004 WL 1773697 at *2-5 (involving the anti-depressant Zoloft); *Dusek*, 2004 WL 2191804 at *2-10 (involving Zoloft); *Ehlis v. Shire Richwood, Inc.*, 233 F.Supp.2d 1189, 1198 (D.N.D.2002) (involving Adderall, a drug used for treatment of ADHD in children); *Abramowitz*, 2006 WL 560639, at *5 (involving pain-management drug Actiq); *see also C.E.R.1988*, 386 F.3d at 270; *Pokorny*, 902 F.2d at 1123; *Kanter v. Warner-Lambert Co.*, 99 Cal.App.4th 780, 794, 122 Cal.Rptr.2d 72 (2002); *Cellucci v. Gen. Motors Corp.*, 550 Pa. 407, 706 A.2d 806, 811 (1998); *Guice v. Charles Schwab & Co.*, 89 N.Y.2d 31, 651 N.Y.S.2d 352, 674 N.E.2d 282, 289 (1996) (cases

finding preemption but not involving the FDCA). (Def. Apotex's Mem. at 8-14; Def. Apotex's Supp. Mem. at 18-24; Def. Apotex's 2nd Supp. Mem. at 2-8).

In response, Plaintiff argues that while generic makers must rely on the innovator manufacturer's labeling and research to get initial approval, once the ANDA is approved, the regulations explicitly permit strengthening of product warning labels. 21 C.F.R. § 314.70(c)(6)(iii)(A), (D); 57 Fed.Reg. 17950, 17961. Thus, he argues the FDCA establishes a floor and not a ceiling with regards to labeling standards. He too cites to numerous cases-but also none by the Third Circuit-that have confronted this exact issue and have concluded that state failure-to-warn claims are not preempted by the FDCA and its attendant regulations. *See, e.g., Hurley v. Lederle Labs. Div. of Am. Cyanamid Co.,* 863 F.2d 1173 (5th Cir.1988) (noting "the great majority of United States district courts which have addressed this issue have ruled against preemption" and citing seventeen previous decisions to that effect); *Laisure-Radke,* 2006 WL 901657 at *3 (involving the anti-depressant Prozac); *McNellis,* Civ. No. 05-1286, 14 (involving the anti-depressant Zoloft); *Witczak,* 377 F.Supp.2d at 729 (involving Zoloft); *Zikis,* Civ. No. 04-8104, 8 (involving Zoloft); *Cartwright,* 369 F.Supp.2d at 887 (involving Zoloft); *In re Paxil Litig.,* [docket #], 2002 WL 31375497, *1 (C.D.Cal.2002) (involving the anti-depressant Paxil). *See also Osburn v. Anchor Labs., Inc.,* 825 F.2d 908, 912-13 (5th Cir.1987) (involving FDA regulations for veterinary drugs, which are very similar, if not virtually identical to the regulations regarding drugs for humans); *Caraker v. Sandoz Pharm. Corp.,* 172 F.Supp.2d 1018, 1032-36 (S.D.Ill.2001) (manufacturer's common law duty

under Illinois law to warn individuals of postpartum lactation-control drug's dangers was not preempted by federal law). (Pl's Response to GSK at 17-18; Pl's Response to Apotex at 6-12 Pl's Supp. Mem. at 12).

Since the Third Circuit has not confronted this issue, any caselaw cited is merely persuasive. That said, these decisions, authored by eminent jurists, are forceful, analytical, and-if the Court believed it was authorized to make the analysis-it might very well agree with them. This Court has concluded not that their analysis itself is wrong, but rather that it is improper for a federal district judge to engage in this analysis in the first place.

First, it is important to note that in contrast to the instant case, those courts had neither (1) a clear *amicus* brief from the FDA addressing the specific facts of the case before it, and representing its judgment and authority that plaintiff's common law claims are impliedly preempted (*Colacicco Amicus*), or (2) an express statement of policy, formally published in the Federal Register, taking the position that state law failure-to-warn claims are preempted by the FDCA (Preemption Preamble). These documents are dispositive to our determination that Plaintiff's claims are preempted.

Second, this is not a case about individual rights or Constitutional interpretation, in which judges have obligations to protect civil liberties, but is essentially a case about economics-whether a drug company should be at risk for damages because of the death of a woman taking its drugs. When Congress established the elaborate system of legislation for the introduction of new drugs, and authorized a federal

agency to implement and police its operation, the resolution of claims arising out of alleged shortcomings in drug instructions and labeling should be as allowed by Congress. Congress has not provided for such claims, and the FDA has taken the position that plaintiff's claims based on state law are inconsistent with its statutory-administrative regimen. Kenneth W. Starr, *Judicial Review in the Post-Chevron Era,* 3 Yale J. on Reg. 283, 308 (1986) ("intrusions not clearly mandated by Congress or the Constitution into the processes and decisions of [a federal agency]" should be avoided because administrative agencies are not subordinate to the federal courts in the organizational structure established by the Constitution).

It is of course true that this Court or any other trial judge with a case such as this could proceed to trial (where a jury would be required to render a verdict based on the same medical judgments considered by the FDA), and appeals by the losing party would wind their way through the court system. However, because preemption is warranted, the case should be dismissed now; if the Court is wrong, Congress can fix this error quickly, and so can the executive branch, by installing different managers at the FDA. Ultimately, this Court believes it is far more desirable that the important issues presented by this case, indeed tragic in its facts, are better addressed by elected officials, legislative and executive, than by appointed judges, a belief which itself has been echoed by the Supreme Court. *See Chevron,* 467 U.S. 837, 104 S.Ct. 2778; Cass R. Sunstein, *Law and Administration After Chevron,* 90 Colum. L.Rev.2071, 2088-90 (1990) ("*Chevron* is best understood and defended as a frank recognition that sometimes interpretation is not

simply a matter of uncovering legislative will, but also involves extratextual considerations of various kinds, including judgments about how a statute is best or most sensibly implemented. *Chevron* reflects a salutary understanding that these judgments of policy and principle should be made by administrators rather than judges."); Laurence H. Silberman, *Chevron: The Intersection of Law and Policy,* 58 Geo. Wash. L.Rev. 821, 823 (1990) ("*Chevron's* importance is its recognition that ... agencies ... maintain a comparative institutional advantage over the judiciary in interpreting ambiguous legislation that the agencies are charged with applying."); Richard J. Pierce, Jr., *The Role of Constitutional and Political Theory in Administrative Law,* 64 Tex. L.Rev. 469, 506 (1985) (noting the *Chevron* Court "recognized that policy choices should be made by the most politically accountable branch of government, and that the judiciary is the least politically accountable branch"). Further, although the facts of *Chevron* may have involved ambiguous terms in a statute, its principles have been consistently carried into the far reaches of administrative law, and governs this case as well. *Geier,* 529 U.S. at 883, 120 S.Ct. 1913; *Chevron,* 467 U.S. at 844, 104 S.Ct. 2778; *Hillsborough County,* 471 U.S. at 714, 105 S.Ct. 2371; *Horn,* 376 F.3d at 180. *See generally,* Scalia, *Judicial Deference, supra.*

Also, the FDA in the *Colacicco Amicus* brief and in the Preemption Preamble-which we have already determined deserves considerable deference-squarely rejected Plaintiff's other arguments. The Preemption Preamble specifically analyzes and dispels the "misunderstanding" cited by numerous lower courts

that FDA labeling requirements represent a minimum safety standard, clarifying that the FDCA "establish[es] both a 'floor' and a 'ceiling.' " Preemption Preamble, 71 Fed.Reg. at 3934-35.

Third, we find compelling Defendant Apotex' argument that, pursuant to the relaxed generic approval process mandated by the Hatch-Waxman Amendments, it was *required* to use verbatim the language of Defendant GSK's warning label during the ANDA application and approval process. Thus, assigning a duty to include a warning different from GSK's approved label inherently conflicts with the FDCA. Additionally, although many courts have held that once the ANDA is approved, 21 C.F.R. § 314.70 explicitly permits unilateral strengthening of product warning labels, the FDA now says otherwise. In its *amicus* brief, the FDA explicitly asserts that "there is no statutory or regulatory provision permitting the manufacturer to make a labeling change to its generic drug without prior FDA approval." *Colacicco Amicus* at 6. *See also* Preemption Preamble, 71 Fed.Reg. at 3934-35. Presumably, this is to insure that the added language is substantiated by scientific data and if not-as would have been the case if Apotex tried to add a label linking paroxetine hydrochloride to suicidality in October 2003-it would have been deemed "misleading" and, thus, in violation of federal law. *Colacicco Amicus* at 15. Therefore, notwithstanding other lower courts' holdings that the plain language of § 314.70 seems to permit pharmaceutical manufacturers to add or strengthen warning without prior FDA approval, we interpret *Geier* to require us to respect the FDA's conclusion that such changes are not allowed, as the FDA is "uniquely qualified" to interpret the regulations

which it is entrusted by Congress to administer. *Geier*, 529 U.S. at 883, 120 S.Ct. 1913. Finally, we agree with the FDA's position that ensuring that warnings be scientifically substantiated is an important public policy. Dissemination of unsupported warnings risks diluting those that are scientifically supported, and/or discouraging safe and effective use of a particular drug. This could deprive patients of efficacious treatment, thereby chilling the drug's otherwise beneficial use. *Colacicco Amicus* at 13.

Accordingly, we find that state tort law which would hold a generic drug manufacturer liable for failing to modify a label when, pursuant to the Hatch-Waxman Amendments to the FDCA, the ANDA approval process required that the labeling be the same as that approved for the innovator drug, and a when the FDA would have deemed any post-approval enhancements "false or misleading," would actually conflict with the FDCA. For these reasons, as well as our conclusion that we must afford deference to the FDA's position that the claims are preempted, we find that Plaintiff's failure-to-warn claims are impliedly preempted.[FN19]

> FN19. While Count XI (survival action), Count XII (wrongful death) and Count XIII (punitive damages) were not the subject of the current motions to dismiss, we now conclude, *sua sponte*, that preemption necessarily bars those claims as well.

B. Effect of Buckman Co. v. Plaintiffs' Legal Committee

Finally, Defendants also urge that *Buckman Co. v. Plaintiffs' Legal Committee* requires that this Court find preemption in this case. We disagree.

In *Buckman*, the Supreme Court held that the FDCA, as amended by the Medical Device Amendments, impliedly preempted the plaintiff patients' state law "fraud-on-the-agency" claims against a manufacturer's regulatory consultant, based on statements allegedly made to the FDA in the course of seeking pre-market approval for orthopedic bone screws. *Buckman*, 531 U.S. at 353, 121 S.Ct. 1012. Defendants argued in their briefs and at oral argument that this case stands for the proposition that the FDCA preempts the negligence *per se* claim at minimum, and possibly all Plaintiff's state tort law claims asserting inadequate warning. (Def. GSK's Mem. at 9; Apotex's Mem. at 25; Def. GSK's Supp. Mem. at 18-19; Apotex' Supp. Mem. at 24-25).

The Court agrees with Plaintiff that *Buckman* is distinguishable. In *Buckman*, the manufacturer of certain orthopedic bone devices hired a consulting company to help the manufacturer "navigat[e] the federal regulatory process." Plaintiffs brought suit not against the manufacturer, but instead alleging the defendant consultant company had defrauded the FDA in obtaining approval for the orthopedic screws. Thus, when the Supreme Court held that the claims were impliedly preempted by the FDCA, it limited this holding to the rationale that *policing fraud upon the FDA* is decidedly a federal function. *Buckman*, 531 U.S. at 347, 121 S.Ct. 1012. Here, there is no "fraud on the FDA" alleged and there is no comparative authority permitting the FDA to police non-compliance with the warning label regulations by virtue of not affirmatively providing stronger warnings. Further, as evidence of the fact that *Buckman* does not usurp all state tort claims, we note

that numerous post-*Buckman* federal cases have rejected the preemption argument for claims based on inadequate warning labels on prescription drugs. *See, e.g., Laisure-Radke,* 2006 WL 901657 at *3; *McNellis,* Civ. No. 05-1286, at 14; *Witczak,* 377 F.Supp.2d at 729; *Zikis,* Civ. No. 04-8104, at 8; *Cartwright,* 369 F.Supp.2d at 887; *In re Paxil,* 2002 WL 31375497, at *1; *Caraker,* 172 F.Supp.2d at 1032-36. Simply stated, *Buckman* is irrelevant to the preemption issues presented in this case.

VII. Issues Arising Under State Law Claims

A. Duty of Care

1. Defendant GSK: No Duty of Care Owed

[7] However, we do not rest our dismissal of GSK on preemption alone. Because we hold that a name brand drug manufacturer does not owe a legal duty to consumers of a generic equivalent of its drug, at least for Defendant GSK, the lack of a duty of care provides a second basis for dismissing all claims against it.

Defendant GSK contends that under Pennsylvania law, "the most essential characteristic of any product liability action ... is that the defendant manufactured or sold the product in question" and because GSK did neither, it had no direct relationship with Plaintiff or his decedent. Thus, GSK argues it owed no duty of care and therefore cannot be liable under any theory. In support of this contention, GSK cites *Foster v. American Home Products,* 29 F.3d 165 (4th Cir.1994) (applying Maryland law), a case in which the Fourth Circuit held that a innovator drug manufacturer does not owe a legal duty to a consumer of a generic drug.

(Def. GSK's Mem. at 3-6; Def. GSK's Reply at 4-5; Def. GSK's Supp. Mem. at 2-3, 7).

Plaintiff responds that Defendant GSK's reliance on *Foster*, based on Maryland law, is inapposite. First, he notes that "direct to consumer" ("DTC") advertising has dramatically expanded since *Foster* was decided, from $242 million in 1994 to approximately $2.38 billion in 2001, which has increased consumers' reliance on name-brand advertising, even if they actually take the generic. Second, in contrast to Maryland, in which foreseeability is the principal determinant of duty, Plaintiff contends Pennsylvania employs a more nuanced duty analysis. Specifically, Plaintiff avers that under the Pennsylvania Supreme Court's analysis in *Althaus v. Cohen*, 562 Pa. 547, 756 A.2d 1166, 1169 (2000), which lays out five distinct factors, including public policy, that must be considered in determining whether a duty of care exists, this Court must allow a jury to find that Defendant GSK owed a duty of care. (Pl's Response to GSK at 4-12; Pl.'s Supp. Mem. at 2-3, 6-7).

In *Althaus*, the Pennsylvania Supreme Court held that the determination of whether a duty exists in a particular case is rooted in public policy and involves the weighing of numerous factors, which include: (1) the relationship between the parties; (2) the social utility of the actor's conduct; (3) the nature of the risk imposed and foreseeability of the harm incurred; (4) the consequences of imposing a duty upon the actor; and (5) the overall public interest in the proposed solution. *Althaus*, 756 A.2d at 1169. However, while *Althaus* and its progeny lay out the general rubric for determining duty, the Pennsylvania courts have not

specifically faced the question of whether a name brand drug manufacturer owes a legal duty to generic brand consumers. Thus, absent clear precedent, this Court must decide how it believes the Pennsylvania Supreme Court would decide the issue.

Having reviewed the caselaw nationwide, it appears that *Foster,* decided by the Fourth Circuit and applying Maryland law, is the single case which has confronted this issue most directly and in most detail. In *Foster,*[FN20] the parents of an infant who died after ingesting a generic drug, sued Wyeth, the manufacturer of the brand-name version of the prescription. *Foster,* 29 F.3d at 167.[FN21] Wyeth moved for summary judgment on all counts, asserting, like GSK, that it could not be held liable under any theory because it did not manufacture or produce the drug taken by the deceased infant. *Id.* After the district court granted the motion for Wyeth on all counts, the case proceeded on appeal to the Fourth Circuit. *Id.* at 168.

> FN20. For a detailed discussion of *Foster,* see Jean A. Brodie, Note, *Foster v. American Home Products Corp.: Tort Liability for Injuries Caused by Someone Else's Product?,* 12 T.M. Cooley L.Rev. 431, 468 (1995).
>
> FN21. The parents had also filed suit against the generic manufacturer, but had initially mistakenly named the wrong company. In their subsequent suit against the proper manufacturer of the generic, the plaintiffs agreed to a dismissal with prejudice for reasons not stated in the record. *Foster,* 29 F.3d at 167.

Specifically before the Fourth Circuit was the question whether the manufacturer of a brand-name prescription drug could be held liable on a negligent misrepresentation theory for an injury caused by a

generic equivalent drug manufactured by another company. *Id.* The court answered "no," reasoning that there is no recognized cause of action based on negligent misrepresentation against one manufacturer for injuries stemming from use of another manufacturer's product. *Id.* Quite simply, the circuit court found that all products liability actions *require* proof that the defendant made the product to which the alleged injuries are attributable. *Id.*[FN22] Further, the *Foster* court held that although the generic drug approval process requires generic manufacturers to initially use the same labeling as the previously approved innovator drug, this does not absolve them of liability for the representations made on their own drugs. *Id.* at 170-71. Moreover, the *Foster* court noted that it would be unfair to use an innovator drug manufacturer's statements regarding its drug as the basis for liability for injuries caused by another manufacturer's drug: while the generic manufacturer reaps the financial benefits of the name brand manufacture's research and "rid [es] on the coattails of its advertising," the innovator drug manufacturer has no control whatsoever over the manufacturing or labeling of the generic substitute. *Id.* at 171. Finally, citing a complete lack of precedent, the *Foster* court concluded that a foreseeability analysis similarly did not lead to the imputation of a duty of care on the innovator drug manufacturer, because to do so would "stretch the concept of foreseeability too far." *Id.* In sum, it found that "Wyeth is under no duty of care to the plaintiffs." *Id.*

FN22. Notably, the district court had considered the negligent misrepresentation claim to be distinct from the negligence, strict liability and breach of warranty claims. While it disposed of the latter three because Wyeth was

> not the manufacturer, the district court refused to do so for the negligent misrepresentation claim. It only granted summary judgment based on plaintiffs' failure to prove reliance on a Wyeth representation, a necessary element of the common law tort of misrepresentation. On appeal, the Fourth Circuit found this distinction to be erroneous, clearly holding that *all* product liability actions require that the defendant have manufactured the product in question. *Id.* at 168.

Notably, the *Foster* decision has encountered widespread acceptance; a review of caselaw reveals that every state and federal district court which has confronted the issue of innovator drug-manufacturer liability has either adopted the *Foster* reasoning or cited *Foster* with approval. *See Tarver v. Wyeth, Inc.*, Civil Action No. 3-04-2036, slip. op. (W.D.La. Apr. 28, 2005) (applying Louisiana law); *Block v. Wyeth, Inc.*, 02-cv-1077, 2003 WL 203067 (N.D.Tex. Jan.28, 2003) (under Texas law); *DaCosta v. Novartis AG*, 01-cv-800, 2002 WL 31957424 (D.Or. Mar.1, 2002) (applying Oregon law); *Christian v. 3M*, 126 F.Supp.2d 951, 958 (D.Md.2001) (applying Maryland law); *Miller v. Bristol-Myers Squibb Co.*, 121 F.Supp.2d 831, 836 (D.Md.2000) (applying Maryland law); *Sharp v. Leichus*, 2004-CA-0643, 2006 WL 515532 (Fla.Cir.Ct. Feb.17, 2006); *Kelly v. Wyeth*, MICV 2003-03314-B, 2005 WL 4056740, slip. op. (Super.Ct.Mass. May 6, 2005); *Sheeks v. Am. Home Prods. Corp.*, No. 02CV337, slip. op. (Dist.Ct.Colo. Oct. 15, 2004); *Sloan v. Wyeth, Inc.*, No. MRS-L-1183-04, slip. op (Super.Ct.N.J. Oct. 13, 2004); *Beutella v. A.H. Robins*, Civil No. 980502372, 2001 WL 35669202, slip. op. (Utah Dist.Ct. Nov. 7, 2001).

While this Court is of course not bound by *Foster* and its progeny, we-like our sister courts across the nation-find it persuasive and adopt its holding. First,

although Maryland law differs slightly from Pennsylvania's as to ascertaining a duty of care and as to the elements of certain product liability theories (e.g., strict liability), it is the same with respect to an essential and elementary characteristic of product liability law: both states require that the defendant manufacture or sell the product in question. *See, e.g. Hahn,* 673 A.2d at 891 (product liability claim can only be brought against "a manufacturer" of the drug in question); *Mellon v. Barre-Nat'l Drug Co.,* 431 Pa.Super. 175, 636 A.2d 187, 191-92 (1993) ("In general, a defendant must be identified as the manufacturer, distributor, or seller of the offending product before the injuries suffered by the plaintiff may be found to be proximately caused by some negligent act or omission of the defendant."). [FN23] Furthermore, even though foreseeability is the principal determinant of duty in Maryland, *Foster* indirectly touches on most, if not all, of the *Althaus* factors. Specifically, we agree that to impose a duty in this case "would be to stretch the concept of foreseeability too far," as GSK cannot reasonably expect that consumers will rely on information they provide when actually ingesting another company's drug. *Foster,* 29 F.3d at 171. Also, we agree that unfair consequences would result if we were to impose a duty upon GSK, when it obtained no benefit from the sale of Apotex's generic equivalent and had no control over the manufacturing or labeling of paroxetine hydrochloride, yet it bore the expense of developing Paxil from which Apotex materially benefits. *Id.* at 170.

FN23. This concept is well-settled under Pennsylvania law. *See, e.g., Soldo v. Sandoz Pharm. Corp.,* 244 F.Supp.2d 434, 524 (W.D.Pa.2003) ("Absent a causal relationship between the *defendant's product* and the

> plaintiff's injury the defendant cannot be held liable on a theory of negligence, strict product liability, or misrepresentation."); *Long v. Krueger, Inc.*, 686 F.Supp. 514, 517 (E.D.Pa.1988) ("In a product liability case, the *plaintiff must identify the defendant as the manufacturer or seller of the offending product* before a plaintiff's injuries may be found to be proximately caused by the negligence of the defendant."); *Klein v. Council of Chem. Ass'ns*, 587 F.Supp. 213, 222-23 (E.D.Pa.1984) (dismissed for failure to state a claim because plaintiff was unable to identify the product(s) that caused his injuries and, in turn, he could not identify which if any of the named defendant manufacturers created the product); *Layton v. Blue Equip. Co. of Can., Ltd.*, 599 F.Supp. 93, 95 (E.D.Pa.1984) (granting summary judgment for defendants because plaintiff did not identify the manufacturer of the lift-jack that allegedly injured her); *Incollingo v. Ewing*, 444 Pa. 263, 282 A.2d 206, 219 (1971) ("companies which *make and sell drugs*... [must be held] to a high degree of responsibility.") (overruled as to another point of law); *Cummins v. Firestone Tire & Rubber Co.*, 344 Pa.Super. 9, 495 A.2d 963, 967-68 (1985) (general rule under Pennsylvania law is that plaintiff *must identify a defendant as the manufacturer or seller of the product* that caused plaintiff's injury before he may establish that the injuries were proximately caused by defendant's negligence and "[a]bsent such identification, there can be no ... liability").

To the extent that Pennsylvania law on the existence of duty requires the additional consideration of public policy, this does not advance Plaintiff's claims against GSK. Contrary to Plaintiff's assertion that this Court is free to divine its own interpretation of public policy, in fact, Pennsylvania courts generally ascertain public policy "by reference to the laws and legal precedents and not from general considerations of supposed public interest." *Prudential Prop. & Cas. Ins. Co. v. Colbert*, 572 Pa. 82, 813 A.2d 747, 752 (2002); *Shick v. Shirey*, 552 Pa. 590, 716 A.2d 1231, 1237 (1998). As Defendant GSK correctly argues,

Pennsylvania courts have recognized the societal importance of new and effective prescription drugs, *Gile v. Optical Radiation Corp.*, 22 F.3d 540, 546 (3d Cir.1994). To encourage this process, the courts have also recognized the need not to unduly burden the pharmaceutical industry with unfettered liability. *Hahn*, 673 A.2d at 890-91 (holding, on policy grounds, that a strict liability claim should not lie against drug manufacturer); *Incollingo v. Ewing*, 444 Pa. 263, 282 A.2d 206, 220 (1971) (holding pharmaceutical *manufacturers* to a high degree of responsibility) (emphasis added).[FN24] In addition to evincing policy, this also suggests the "social utility" and "consequences of imposing a duty" prongs in *Althaus* weigh against finding a duty owed by GSK. Additionally, the courts and legislature of the Commonwealth have evinced a policy of deference to any well-defined public policy embodied by federal law. *See State Farm Mut. Auto. Ins. Co. v. Foster*, 585 Pa. 529, 889 A.2d 78, 80-81 (2005) ("the legislative concern for the increasing cost of automobile insurance is the public policy to be advanced by statutory interpretation of the MVFRL"); *In re Estate of Wagner*, 584 Pa. 49, 880 A.2d 620, 626 (2005) (holding that the statute creating "child death reviews" to be conducted by the Department of Public Welfare clearly expressed public policy to identify remedial possibilities and better safeguard children, which purpose could not be accomplished if agencies feared making discoverable admissions that could lead to liability, dictated outcome that audits could not be available to plaintiffs as discovery); *see also Acands, Inc. v. Travelers Cas. & Sur. Co.*, 435 F.3d 252, 258 (3d Cir.2006) ("courts may refuse to enforce arbitration awards that violate well-defined public policy as embodied by federal law."). More

specifically, like the federal courts discussed above, the Pennsylvania courts and legislature have shown deference to the FDCA. They have viewed the FDCA as indicia of a federal policy that in the area of prescription drugs, the FDA is uniquely qualified to decide whether state law stands as an obstacle to the objectives of Congress. *See White v. Weiner,* 386 Pa.Super. 111, 562 A.2d 378, 383 (1989) (stating that "our legislature unequivocally has expressed a policy of deference to the federal scheme in the area of drug labeling ... and we can ascertain no reason not to extend that policy to civil cases raising misbranding claims"); *see also Horn,* 376 F.3d at 171 (applying Pennsylvania law); *Gile,* 22 F.3d at 546 (applying Pennsylvania law). Further, the fact that Congress created the FDA in the first place, and the statutory scheme embodied in the FDCA, demonstrates that it believes the public interest is best served by the FDA's weighing of the risks and benefits of a particular prescription drug. These federal policies, when analyzed in conjunction with the other factors under *Althaus,* militate against finding a duty of care owed by GSK.

> FN24. In contrast, we reject Plaintiff's contention that Pennsylvania's policy of holding pharmaceutical *manufacturers* to a high degree of care supports imputing a duty of care to GSK. *Incollingo,* 282 A.2d at 219. In fact, *Incollingo* merely reiterates that idea that "companies which *make and sell drugs*... [must be held] to a high degree of responsibility ... for any failure to exercise vigilance commensurate with the *harm which would be likely to result* from relaxing it." *Id.* (emphasis added). Thus, *Incollingo* supports the idea, as discussed *supra,* that the actual maker of the drug-in this case Apotex-should be held to have a duty of care to consumers. It is erroneous to assert that *Incollingo* supports the proposition that public policy is served by

holding GSK liable for injuries stemming from use of Apotex's product.

Like in *Foster,* Plaintiff in this case invites this Court to drastically expand the boundaries of Pennsylvania tort law without precedent or policy to support his position.[FN25] We believe the Supreme Court of Pennsylvania would not accept this invitation, and accordingly, we decline to do so as well. Thus, this Court holds that under Pennsylvania law, there is no duty of care owed by a brand-name prescription drug manufacturer to a plaintiff allegedly injured by a generic equivalent drug manufactured by another company. Thus, even if this Court's conclusion regarding preemption were found to be improper, the claims against Defendant GSK must still be dismissed.[FN26]

FN25. In *Bilt-Rite Contractors, Inc. v. Architectural Studio,* 581 Pa. 454, 866 A.2d 270, 285 (2005), the Pennsylvania Supreme Court held that an architect who supplied information and services to a contractor for pecuniary gain, knowing it would be relied upon by the contractor in bidding on a construction project, would be held to have a duty of care even though privity of contract was lacking. *Id.* Further, the court held that the economic loss rule does not bar recovery for negligent misrepresentation in such a case. *Id.* Plaintiff argues for a broad reading of *Bilt-Rite,* contending that it supports finding that GSK owed a duty of care, even though it did not manufacture the drug in question. The Court understands *Bilt-Rite* to have a narrower holding, adopting § 552 of the Restatement of Torts (Second) only as it applies to "architects and other design professionals." *Bilt-Rite,* 866 A.2d at 286. Further, "given the important reliance placed upon ... professional services," the *Bilt-Rite* court also recognized the importance of the fact that the seller was a professional. Finally, *Bilt-Rite* was confined to a situation where purely economic damages were alleged, and thus the

> holding was a specific exception to the economic loss rule. Here, Defendant GSK is not in the business of designing and/or building homes, the various policy reasons behind liability for "design professionals" are simply inapplicable to a drug manufacturing company, and economic loss is not at issue. In sum, *Bilt-Rite* is inapplicable to the present case.
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> FN26. Again, while Counts XI-XIII were not the subject of Defendants' motions to dismiss, the lack of a duty of care owed by GSK bars those claims as well.

2. Defendant Apotex: Duty of Care Owed

[8] Defendant Apotex asserts that it was not responsible for the form or substance of the labeling connected with paroxetine hydrochloride, and therefore it too did not owe a duty of care to Plaintiff that would give rise to liability against it. For the reasons that follow, this contention must be rejected.

In making this argument, Apotex focuses on the H-W Amendments, which allow a generic maker to rely on the innovator's testing and require it to use identical labeling as the innovator in order to obtain FDA approval. Thus, Apotex argues that, "like a pharmacist who assembles the components of a drug prescribed by a physician," its only duty with respect to labeling was to attach a label which was the same as that approved for Paxil, which it did. As for a more generalized duty, Apotex cites to foreseeability and public policy, two critical factors in the *Althaus* duty analysis. It urges: (1) the H-W Amendments made it unforeseeable that it could be held liable for inadequacies in labels it did not create, and (2) the H-W Amendments are a clear policy expression by Congress to avoid imposing a duty on generic manufacturers. Further, distinguishing *Foster*,

Apotex takes the position that because the generic manufacturer was no longer a party to the suit when the case was decided, the Fourth Circuit's holding that the generic manufacturer owes a duty of care to consumers who ingest its drug is mere *dicta*. (Def. Apotex's Mem. at 5-9; Def. Apotex's Supp. Mem. at 7-18, 25-29).

Plaintiff counters that quite simply, Apotex, like all product manufacturers, cannot escape the duty it owes to all its consumers. This is because it has a very direct relationship with them: it makes and labels the drug they take. (Pl.'s Resp. at 4-6).

In deciding whether Apotex owed Plaintiff a duty of care, we address the *Althaus* factors in turn. As a threshold matter, Apotex challenges the first *Althaus* factor, the relationship between the parties. Citing *Makripodis v. Merrell-Dow Pharmaceuticals Inc.*, 361 Pa.Super. 589, 523 A.2d 374, 377 (1987), in which the court held that a pharmacist who properly dispenses a prescription ordered by a physician owes no duty to consumer, Apotex suggests that similarly, it is merely an intermediary who passed along the warning label already prepared by GSK. This Court believes that this endeavor to liken itself to a mere middleman misses the mark. We agree with Plaintiff that Apotex's attempts to distance itself from consumers of its drugs obfuscates the direct relationship that it has with persons who ingest the very drug *Apotex* makes and *Apotex* sells: paroxetine hydrochloride, with the very labels *Apotex* attaches to it. Further, that all manufacturers owe a duty of care to their customers is among the most basic tenets of product liability law, and Apotex cites no caselaw to the contrary. *See, e.g., Hahn*, 673 A.2d at 891; *Incollingo*, 282 A.2d

at 219. Thus, we find this direct relationship, if not dispositive, weighs heavily in favor of finding a duty.

Moreover, we find the *Foster* court's discussion of generic manufacturer liability-specifically foreseeability and public policy-compelling. While it is true that the ANDA process requires generic manufacturers to use the same labeling as the previously approved innovator drug, we cannot agree that this absolves them of liability for the representations made on their own drugs. That basic tort concepts always hold a manufacturer liable for its products makes liability based on inadequate labeling foreseeable to Apotex. Nor can we agree that the H-W Amendments are a clear policy expression by Congress to avoid imposing a duty on generic manufacturers or made it unforeseeable that Apotex could be held liable for inadequacies in its *own* labels. If that was Congress' intent, it or the FDA would have said so. Moreover, Plaintiff's argument that this portion of *Foster* is *dicta* is irrelevant, as we have already acknowledged that *Foster* has no controlling effect on this court. Whether *dicta* or not, we look to this part of *Foster* for its *reasoning,* and because this reasoning is well-articulated and persuasive, this Court adopts it.

Finally, the last two *Althaus* factors-the social utility of the actor's conduct, and the consequences of imposing a duty upon the actor-do not weigh against finding a duty owed by Apotex. While one could argue that there is social utility in making less-expensive, generic substitutes available to the public, this Court is mindful of the fact that Apotex is still a business, manufacturing drugs like paroxetine hydrochloride not for some altruistic reason, but to realize a profit.

Apotex reaps the financial rewards of selling paroxetine hydrochloride, and it cannot hide from liability by crying regulatory foul. Also, the economic consequences of imposing a duty upon Apotex are marginal, given that a duty of care is imposed on all product manufacturers. *See, e.g., Hahn,* 673 A.2d at 891; *Incollingo,* 282 A.2d at 219. Accordingly, we hold that Apotex owed a duty of care to Plaintiff and Plaintiff's decedent, sufficient to give rise to liability against it.

B. Learned Intermediary Doctrine

A third ground cited by Defendants for dismissing the entire complaint, which we reject at this stage of the litigation, is the "learned intermediary" doctrine ("LID"), under which a drug manufacture's liability is based on its warning labels targeted at doctors, not consumer-patients. (Def. Apotex's Mem. at 16; Def. GSK's Supp. Mem. at 22-26; Def. Apotex's Supp. Mem. at 37-40). Plaintiff counters that the LID does not apply because: (1) he has plead that Defendants failed to provide adequate warnings to among others, decedent's treating and/or prescribing physician, Compl. at ¶ 86, and (2) the doctrine requires an analysis of the adequacy of the warnings, a question of fact which cannot be determined at this early stage. Further, citing *Perez v. Wyeth Labs.*, 161 N.J. 1, 734 A.2d 1245 (1998), Plaintiff counters that a direct-to-consumer ("DTC") advertising exception should apply to the LID. *Perez*, 734 A.2d at 1257 (concluding that, when mass marketing seeks to influence a patient's choice of a prescription drug, a pharmaceutical manufacturer should not be unqualifiedly relieved of a duty of care and thus adopting the DTC advertising exception to the LID).

physicians to adequately advise their patients. *See, e.g., Amore v. G.D. Searle & Co.*, 748 F.Supp. 845, 850 (S.D.Fla.1990). Thus, as Plaintiff correctly argues, the Court must undertake an analysis of the sufficiency of the warnings. *Makripodis*, 523 A.2d at 378 ("an action against a drug manufacturer based upon inadequate warnings, the issue to be determined is whether the warning, if any, that was given to the prescribing physicians was proper and adequate."). *See also Brecher v. Cutler*, 396 Pa.Super. 211, 578 A.2d 481, 485 (1990). This cannot be done at the 12(b)(6) stage because the representations of the decedent's doctor as to whether, if at all, she relied upon these warnings is not in the record.[FN28] Accordingly, the applicability of the learned intermediary doctrine is more appropriate in a motion for summary judgment.[FN29] *See, e.g., Cahill v. Miles, Inc.*, 91-cv-1966, 1992 WL 110537 (E.D.Pa.1992) (summary judgment entered for drug manufacturer where record demonstrated that defendant warned of specific adverse side effects suffered by plaintiff); *Ferrara v. Berlex Labs., Inc.*, 732 F.Supp. 552, 555 (E.D.Pa.1990) (same); *Brecher*, 578 A.2d at 485 (same); *Taurino v. Ellen*, 397 Pa.Super. 50, 579 A.2d 925, 927-28 (1990) (LID bars products liability claim on summary judgment where adequacy of warning was conceded by plaintiff). Accordingly, this Court will not dismiss any of Plaintiff's claims at this juncture based on the learned intermediary doctrine.[FN30]

FN28. We consider the exhibits to Plaintiff's amended complaint which demonstrate that there was no warning as to an association between the drug and suicidality in October 2003. Specifically, plaintiff attached the "Prescribing Information" available in July 2003 for Paxil/paroxetine hydrochloride (Amd. Compl., Exhibit A),

as well as the 2003 description of paroxetine hydrochloride available through Micromedex (Amd. Compl., Exhibit C). While the general rule is that a court may not consider evidence outside the pleadings for a 12(b)(6) motion without converting it to a summary judgment motion, the Third Circuit has held that a court may properly consider a concededly authentic document upon which the complaint is based. *Pension Benefit Guar. Corp.*, 998 F.2d at 1196. First, where Plaintiff's entire complaint is based on failure-to-warn, clearly the warnings themselves are documents upon which the complaint is based. Second, it has never been disputed by the parties that no such warning was included in October 2003. *Id.* However, neither evidence as to what Defendants knew nor the extent to which decedent's doctor relied upon these warnings is in the record.

FN29. We note that generally, whether a particular warning is "adequate" is a question of fact to be resolved by a jury. *See Dougherty v. Hooker*, 540 F.2d 174, 182 (3d Cir.1976). Defendants, however, argue that adequacy of the warning is a question of law and cite *Davis v. Berwind Corp.*, 547 Pa. 260, 690 A.2d 186, 190 (1997) and *Demmler v. SmithKline Beecham Corp.*, 448 Pa.Super. 425, 671 A.2d 1151, 1154 (1996) in support of that proposition. (Def. Apotex' Supp. Mem. at 38; Def. GSK's Supp. Mem. at 24). However, Defendants oversimplify the principles articulated by those courts. In fact, both cases state that the adequacy question is only *initially* a question of law, citing precedents that demonstrate that the full analysis requires a two-step inquiry. The court must first determine as a threshold issue whether recovery would possibly be justified under the plaintiff's version of the facts-e.g. the question of law. *Mackowick v. Westinghouse Elec. Corp.*, 525 Pa. 52, 575 A.2d 100, 103 (1990). It is ultimately the trier of fact that must decide whether a particular warning was adequate based on the particular facts of the case-e.g. the actual adequacy question is of fact. *Id.* at 103. Further, "[g]enerally, expert medical testimony is required to determine whether the drug manufacturer's warning to the medical community is adequate," which we do not have at the motion to dismiss stage. *Demmler*, 671 A.2d at 1154.

FN30. If we reached the merits of the LID issue, any direct-to-consumer ("DTC") advertising exception would likely not apply. This is because, in the eight years since *Perez*, the New Jersey Supreme Court case making an exception to the LID for direct-to-consumer advertising, was decided, no state has joined New Jersey. *In re Norplant Contraceptive Prods. Liab. Litig.*, 165 F.3d 374, 377 (5th Cir.1999) (holding that DTC exception to the learned intermediary doctrine should not be created); *In re Meridia Prods. Liab. Litig.*, 328 F.Supp.2d 791, 812 n. 19 (N.D.Ohio 2004) (same). Pennsylvania courts that have considered the issue have expressly rejected the argument. *See Heindel v. Pfizer, Inc.*, 381 F.Supp.2d 364, 378 (D.N.J.2004) (applying PA law); *ex rel. Lennon v. Wyeth-Ayerst Labs., Inc.*, 2001 WL 755944, *2 (Pa.Super. June 14, 2001); *Albertson v. Wyeth Inc.*, 63 Pa. D. & C. 4th 514, 539, 2003 WL 21544488, *11 (Pa.Com.Pl.2003) (although Wyeth engaged in direct-to-consumer advertising, defendant's preliminary objections were sustained because pursuant to the learned intermediary doctrine, defendants had no duty to disclose any information directly to plaintiff); *Luke v. Am. Home Prods. Corp.*, 1998 WL 1781624, *4-5 (Pa.Com.Pl.1998) (same). Thus, absent an intervening change in the applicable law, in this Court's view, Pennsylvania law does not provide any exception to the LID based on direct-to-consumer advertising.

C. Reach of Hahn v. Richter

[11] Finally, Defendants argue that in addition to barring Plaintiff's strict liability claim, the broad holding announced by the Pennsylvania Supreme Court in *Hahn v. Richter*, 543 Pa. 558, 673 A.2d 888, 891 (1996), precludes all Plaintiff's claims except those based in negligence. (Def. GSK's Supp. Mem. at 6; Def. Apotex's Supp. Mem. at 11-12). We agree with this proposition. At least with regard to Plaintiff's non-negligence claims, it provides another basis for dismissal.

In *Hahn*, in barring a strict liability claim against a manufacturer of a prescription drug, the Pennsylvania Supreme Court broadly held that "where the adequacy of warnings associated with prescription drugs is at issue, the failure of the manufacturer to exercise reasonable care to warn of dangers, i.e., the manufacturer's negligence, is the only recognized basis of liability."*Hahn*, 673 A.2d at 891. That is, the court held that because prescription drugs are inherently dangerous, a drug manufacturer only has the duty to exercise reasonable care to inform its intended user of the qualities that make it dangerous. *Id.* at 890 (adopting comment k of the Restatement (Second) of Torts § 402A, which denies application of strict liability to "unavoidably unsafe products" such as prescription drugs and finding § 388, which applies to "chattel known to be dangerous for intended use," to provide the proper standard of care); *see also Mazur*, 964 F.2d at 1353-55 (interpreting *Incollingo* and *Baldino* as requiring a prescription drug manufacturer's liability for failure-to-warn rest on negligence, not strict liability); *Baldino*, 478 A.2d at 810; *Incollingo*, 282 A.2d at 220 n. 8.

While Plaintiff admitted on the record at oral argument that all his claims were based on Defendant's failure-to-warn, Plaintiff nonetheless argues that, in fact, *Hahn* does not control because that court presumed the products were marketed with *proper warnings*, whereas here Plaintiff *challenges* the adequacy of the warnings. (Pl's Response to GSK at 18-19; Pl's Supp. Mem. at 3-5). We find this contention to be without merit. First, the court's broad statement that negligence is the only

recognized basis of liability any time "where the adequacy of warnings associated with prescription drugs *is at issue* " unambiguously demonstrates the holding applies to all failure-to-warn claims, which inherently call into question the adequacy of prescription drug warnings. Second, the *Hahn* court did not just carelessly pronounce a broad holding. Instead, it relied on a well-developed line of cases, including *Mazur,Incollingo,* and *Baldino,* to come to its conclusion. Also, and importantly, the court took great pains to explain *why* failure to exercise reasonable care is the only cause of action that should be permitted for claims which are based on failure-to-warn. Quoting comment k of the Restatement (Second) of Torts § 402A, the court reasoned that prescription drugs "supply the public with ... apparently useful and desirable product[s]," which protect against serious and even deadly diseases. *Hahn,* 673 A.2d at 890, n. 2. This, explained the court, "fully justifie[s]" the marketing and use of prescription drugs, "notwithstanding the unavoidable high degree of risk which they involve." *Id.* Third, *Hahn's* authority for this proposition has not been questioned.

We therefore hold that *Hahn* requires us to dismiss Count IX (strict liability), as well as all of Plaintiff's remaining claims except the four that sound in negligence: negligent misrepresentation (Count IV), negligent infliction of emotional distress (Count VI), negligence (Count VII), and negligence per se (Count VIII). Accordingly, Count II (breach of implied warranty), Count III (fraud by intentional misrepresentation and violation of New York consumer protection law), Count V (intentional

infliction of emotional distress), and Count IX (strict products liability) must be dismissed. [FN31]

FN31. *Hahn* would also bar Plaintiff's original Count I (breach of express warranty), which Plaintiff voluntarily withdrew at oral argument. However, as Plaintiff's Amended Complaint does not reflect this, we want to clarify that even had Plaintiff not dropped it, the breach of express warranty claim (Count I) would not survive anyway.

D. Individual Causes of Action

Assuming *arguendo* that Plaintiff's claims were not barred by preemption, lacking duty of care, and/or the reach of *Hahn*, or this Court's holding as to any or all of those issues were found to be erroneous, Defendants would have to respond to the following arguments pertaining to Plaintiff's individual causes of action. We therefore address each seriatim.

1. Non-negligence Claims

a. Breach of Implied Warranty (Count II)

[12] First, citing the Pennsylvania Superior Court's decision in *Makripodis v. Merrell-Dow Pharmaceuticals Inc.*, 361 Pa.Super. 589, 523 A.2d 374 (1987), Defendant Apotex contends that a claim for breach of implied warranty is not available in cases involving prescription drugs under Pennsylvania law. (Def. Apotex's Mem. at 17). Plaintiff argues his implied warranty claim is viable, urging that *Makripodis* can be distinguished in that it involved a claim against a pharmacy, not a drug manufacturer. (Pl's Response to Apotex at 14).

In dismissing a claim for the implied warranty of merchantability against a retail pharmacist, the *Makripodis* court broadly stated that "the very nature of prescription drugs ... precludes claims for breach of the implied warranty of merchantability." *Makripodis,* 523 A.2d at 377. *See also Murray v. Synthes, U.S.A., Inc.,* 1999 WL 672937, *9 (E.D.Pa. Aug.23, 1999) (relying on *Makripodis,* refusing leave to amend complaint to add an implied warranty claim for prescription medical device). The court reasoned this is because a generalized warranty is not appropriate given that each person for whom a drug is prescribed "is a unique organism who must be examined by a physician who is aware of the nature of the patient's condition as well as the medical history of the patient." *Makripodis,* 523 A.2d at 377.

We concur with Defendants that *Makripodis* bars Plaintiff's implied warranty claim. As a court sitting in diversity, we must apply state law. Here, the Superior Court unambiguously held that persons or entities providing prescription drugs can not be held liable for the breach of implied warranty. Further, we find Plaintiff's contention that *Makripodis* does not apply because the case involved a claim against a pharmacy instead of a drug manufacturer to be without merit. The *Makripodis* court based its decision not on who the defendant was, but rather on the inherently dangerous "nature of prescription drugs." *Id.* It is precisely because of the risks posed that such drugs may be obtained only upon the prescription of a licensed physician and that imposition of a warranty of fitness for ordinary purposes is inappropriate. Accordingly, this Court must preclude Plaintiff's claim for breach of the implied warranty of merchantability. Even if

Plaintiff's complaint was not otherwise barred, Count II would still be dismissed.

b. Fraud by Intentional Misrepresentation and Violation of New York Consumer Protection Act (Count III)

In his Amended Complaint, Plaintiff consolidated the two prior Counts III and X (asserted against both Defendants) into a single new Count III, which sets forth both fraud and violation of New York consumer protection law claims against Defendant GSK only. GSK asserts that both must be dismissed. For the reasons that follow, we disagree that the fraud portion should be dismissed, but agree as to the New York Consumer Protection portion of the count.

i. Fraud

[13][14] The elements of fraud by intentional misrepresentation under Pennsylvania law are: (1) a representation; (2) which is material to the transaction at hand; (3) made falsely, with knowledge of its falsity or recklessness as to whether it is true or false; (4) with the intent of misleading another into relying on it; (5) justifiable reliance on the misrepresentation; and, (6) the resulting injury was proximately caused by the reliance. *Murray*, 1999 WL 672937 at *3; *Bortz v. Noon*, 556 Pa. 489, 729 A.2d 555, 560 (1999); *Gibbs v. Ernst*, 538 Pa. 193, 647 A.2d 882, 889 (1994). The tort of intentional non-disclosure has the same elements, except that in the case of an omission, the party intentionally conceals something rather than making an affirmative misrepresentation. *Bortz*, 729 A.2d at 560.

Defendant GSK argues that Plaintiff's fraud claim lacks the required particularity under F.R. Civ. P. 9(b). Specifically, Defendant GSK asserts the fraud claim must be dismissed because Plaintiff has failed to allege that decedent's prescribing physician relied on any particular statement or information provided by GSK. (Def. GSK's 3rd Supp. Mem. at 2-4).

In contrast to the original Complaint, Plaintiff's Amended Complaint includes numerous specific allegations that all information available about Paxil or its generic equivalent was disseminated by GSK, and that this information was justifiably relied upon by the decedent and her physician. This specificity can be found in the following paragraphs of the Amended Complaint:

28. During [a conversation the physician had with Mrs. Colacicco about the risks of taking paroxetine], Lois was advised that there were no "obvious interactions" between paroxetine and Lorazepam "identified in Micromedex," which is a healthcare research engine that provides drug summaries for physicians.

32. Any and all knowledge that Lois Colacicco's physicians possessed concerning Paxil came from the following sources, which either contained or were the direct result of GSK's manipulated data, material misrepresentations and omissions, and inadequate warnings concerning Paxil: [the 2003 Physicians Desk Reference, the Micromedex, GSK's sales representatives, GSK's website, and GSK's advertisements].

35. When Lois Colacicco's ... physicians decided to prescribe Paxil ... they *based their decisions solely upon the aforesaid manipulated data, false promotion and incomplete warnings.*

36.... There was no information available at that time about the drug that Lois Colacicco was taking other than what had been promulgated and disseminated by GSK.

37. Lois Colacicco ... and her ...*physicians justifiably relied upon all of the information* that had been promulgated and disseminated by GSK....

Amended Compl. at ¶ 28, 32, 35-37 (italics added). Thus, based on the allegations alone, had the claims against GSK not been dismissed earlier for preemption and lack of a duty of care, and had we not found that *Hahn* precluded Plaintiff's non-negligence claims, the fraud portion of Count III would survive.

ii. Violation of New York Consumer Protection Law

Plaintiff also alleges in Count III that "by engaging in deceptive acts and practices and false advertising," Defendant GSK violated section 349 of the New York Consumer Protection Law. Amd. Compl. at ¶ 40; N.Y. Gen. Bus. Law § 349.

[15] A prima facie case for recovery under section 349 of the statute for "deceptive acts or practices" requires a showing that defendant is engaging in an act or practice that is deceptive or misleading in a material way and that plaintiff has been injured by reason thereof. *Oswego Laborers' Local 214 Pension Fund v.*

Marine Midland Bank, 85 N.Y.2d 20, 25, 623 N.Y.S.2d 529, 647 N.E.2d 741 (1995). *See also Leider v. Ralfe,* 387 F.Supp.2d 283, 292 (S.D.N.Y.2005). The allegedly deceptive acts, representations or omissions "must be misleading to a reasonable consumer." *Oswego,* 85 N.Y.2d at 26, 623 N.Y.S.2d 529, 647 N.E.2d 741. Finally, a claim under the New York consumer protection law requires proof that the defendant's acts are directed at consumers. *Id.; Goshen v. Mutual Life Ins. Co. of N.Y.,* 98 N.Y.2d 314, 746 N.Y.S.2d 858, 774 N.E.2d 1190, 1196 (2002).

[16] Although not pleaded by Plaintiff, to assert a cause of action for false advertising under section 350, a plaintiff must demonstrate that the advertisement: (1) had an impact on consumers at large; (2) was deceptive or misleading in a material way; and (3) resulted in injury. *Andre Strishak & Assocs., P.C. v. Hewlett Packard Co.,* 300 A.D.2d 608, 609, 752 N.Y.S.2d 400 (N.Y.App. Div., 2d Dep't 2002). In determining whether an advertisement is "false" within the meaning of the statute prohibiting false advertising, the test is whether the advertisement is likely to mislead a reasonable consumer acting reasonably under the circumstances. *Id.* Additionally, reliance is a element of a claim under section 350. *Leider,* 387 F.Supp.2d at 292. Otherwise, while specific to false advertising, the standard for recovery under N.Y. Gen. Bus. Law § 350 is identical to N.Y. Gen. Bus. Law § 349. *Goshen,* 746 N.Y.S.2d 858, 774 N.E.2d at 1195.

First, Defendant GSK contends that insofar as Plaintiff alleges that GSK engaged in false advertising, that portion of Plaintiff's claim should be dismissed because: (1) false advertising claims fall

under N.Y. Gen. Bus. Law § 350, and (2) Plaintiff has not plead under section 350 or alleged the required reliance on any specific advertisement. Second, while not entirely clear, GSK appears to argue that the New York Consumer Protection Law is inherently inconsistent with the learned intermediary doctrine. Finally, citing *Gray v. Seaboard Securities, Inc.*, 14 A.D.3d 852, 788 N.Y.S.2d 471, 472 (N.Y.App.Div.2005), GSK suggests that inadequate warning claims are not actionable under the consumer protection law because they are analogous to securities violations, for which New York law provides no relief. (Def. GSK's 3rd Supp. Mem. at 4-6).

Plaintiff counters that he sufficiently plead actual reliance on GSK's materials, and that Defendant's contention that its conduct was not aimed at consumer-patients, or that recovery under state consumer protection laws is somehow barred by the learned intermediary doctrine, is belied by the very nature of "direct-to-consumer" advertising. Further, Plaintiff attempts to distinguish *Gray,* noting that court sought to avoid allowing additional protections beyond those afforded under the federal Securities Exchange Act, while the FDCA offers no such protection. (Pl's Response to Apotex at 19-20; Pl's 3rd Supp. Mem. at 4-5).

To the extent that Plaintiff has accused GSK of "engaging in false advertising," while we find that Plaintiff sufficiently plead actual reliance, we agree that this allegation necessarily must fall under N.Y. Gen. Bus. Law section 350.[FN32] Plaintiff improperly plead his entire Count alleging violation of the New York Consumer Protection Law under section 349.

Thus, the portion of Plaintiff's Count III alleging false advertising under New York's Consumer Protection Law must be dismissed. However, even if he had alleged a violation of section 349, it would still be sufficient.

> FN32. GSK acknowledges that some caselaw suggests that a false advertising claim can be brought under either section 349 or section 350 (but provided no citations to this effect). However, it argued that even if there are any, this interpretation is erroneous as this would render section 350 totally superfluous. Plaintiff did not address this contention at all. This court reviewed the caselaw and found that while some New York courts have permitted advertising claims to be brought under section 349, they have only done so when the complaint alleges that the advertising itself is was a "deceptive practice," such that the claim may fit under section 349. *See, e.g. B.S.L. One Owners Corp. v. Key Intern. Mfg., Inc.*, 225 A.D.2d 643, 640 N.Y.S.2d 135, 136 (App.Div.1996) ("defendants engaged in *deceptive practices in the advertisement* " of their products) (emphasis added). Further, such false advertising claims have also been brought under section 350, and not 349 alone. *Id. See also State v. Middletown Beef Co.*, 84 A.D.2d 834, 444 N.Y.S.2d 184, 184 (App.Div.1981). Thus, these cases support Defendant GSK's contention that filing a false advertising claim under 349 alone is not permissible, as it would render section 350 totally superfluous. Accordingly, when, whereas here, a plaintiff pleads false advertising pursuant to only one section of the New York Consumer Protection statute, the allegation necessarily must fall under N.Y. Gen. Bus. Law section 350.

[17] As to Defendant's other objections, we agree that the learned intermediary doctrine also precludes Plaintiff's claim under the consumer protection statute. While the New York courts have yet to confront this specific issue, we believe our holding is entirely consistent with both the statute and the

doctrine. This is because the consumer protection statute forbids deceptive acts or practices likely to mislead a reasonable *consumer*, specifically requiring proof that the defendant's acts are directed at consumers, *Goshen*, 746 N.Y.S.2d 858, 774 N.E.2d at 1196; *Oswego*, 85 N.Y.2d at 26, 623 N.Y.S.2d 529, 647 N.E.2d 741, while the LID dictates that all pharmaceutical information is directed at *physicians, not consumer-patients.*[FN33] Applying other state consumer protection statutes, other courts have come to the same logical conclusion that the statute and the doctrine are inherently inconsistent with one another. *See, e.g., Heindel*, 381 F.Supp.2d at 384 (applying Pennsylvania law, concluding that the LID bars plaintiff's consumer protection claim). Moreover, we find compelling the argument that *Gray* is analogous to the facts at hand. While the federal law at issue differs, both securities and prescription drug labeling are highly regulated by the federal government, a fact relied upon by the *Gray* court. Further, like securities, prescription drugs are not available in the same manner as usual consumer products, also a key component of the *Gray* court's reasoning.

FN33. We note that the LID is applied with equal force in New York, where it is referred to as the "informed intermediary" doctrine, as in Pennsylvania. *Lindsay v. Ortho Pharm. Corp.*, 637 F.2d 87, 91 (2d Cir.1980); *Krasnopolsky v. Warner-Lambert Co.*, 799 F.Supp. 1342, 1346 (E.D.N.Y.1992); *Martin v. Hacker*, 83 N.Y.2d 1, 607 N.Y.S.2d 598, 628 N.E.2d 1308, 1311 (1993); *Bukowski v. CooperVision, Inc.*, 185 A.D.2d 31, 592 N.Y.S.2d 807 (N.Y.App. Div.3d Dep't 1993) (under New York law, all applying the "informed intermediary" doctrine in fixing the scope of liability of manufacturers or sellers for their alleged failure-to-warn of the risks associated with a prescription drug).

In sum, even if we did not conclude *Hahn* barred Plaintiff's non-negligence claims, and that all claims against GSK were dismissed for want of a duty and preemption, the consumer protection portion of Count III would still be dismissed.

c. Infliction of Emotional Distress (Counts V and VI)

Both Defendants next argue that Plaintiff has no right to recover for infliction of emotional distress under either a negligent [FN34] or intentional theory, because both torts require evidence of immediate proximity to the conduct such that it and its consequences are sensorally observed. (Def. GSK's Mem. at 8-9; Def. Apotex's Mem. at 20-23). The Court agrees.

> FN34. Although the negligent infliction of emotional distress claim obviously sounds in negligence (the remainder of which such claims are discussed in Part VII.D.2, *infra*), we choose to discuss it with the intentional infliction of emotional distress claim for ease of reference.

[18] The tort of intentional infliction of emotional distress ("IIED") is defined as: "extreme and outrageous conduct [that] intentionally or recklessly causes severe emotional distress to another." *Hoy v. Angelone*, 554 Pa. 134, 720 A.2d 745, 753 (1998). Where such conduct is directed at a third person, the actor can only be subject to liability for causing emotional distress to a member of such person's immediate family *who is present* at the time. *Taylor v. Albert Einstein Med. Ctr.*, 562 Pa. 176, 754 A.2d 650, 653 (2000) (emphasis added). Similarly, the

Pennsylvania Supreme Court has explicitly held that a showing of the contemporaneous observation of the injury of a close relative is required for a negligent infliction of emotional distress ("NIED") claim. *Brooks v. Decker*, 512 Pa. 365, 516 A.2d 1380, 1382 (1986) (father who came upon scene of accident after his son was struck by an automobile failed to state a claim for NIED because he did not witness the accident).

[19] Here, it is undisputed that Plaintiff came upon his wife's body after she had committed suicide. Whatever act or omission was allegedly undertaken by Defendants did not occur in Plaintiff's presence, which is required to establish the tort of infliction of emotion distress under either theory when it involves conduct directed at a third party. Plaintiff argues, however, that the *reasoning* articulated by Pennsylvania courts in requiring presence is that, in the absence of knowledge of the injury beforehand, the third party has no buffer against the full impact of observing the scene. Thus, he asserts that so long as the third party contemporaneously observes the *result* of the alleged intentionally outrageous or negligent conduct and has no warning of the incident before coming on the scene, the party sufficiently states a claim for infliction of emotional distress. Since he had no pre-warning of and thus no buffer against the full impact of observing the deceased Mrs. Colacicco after her suicide, Plaintiff therefore asserts both his IIED and NIED claims should survive this motion to dismiss. (Pl's Response to GSK at 14-17; Pl's Response to Apotex at 16-17).

Plaintiff misconstrues the caselaw, which clearly requires presence for both IIED and NIED. Both *Mazzagatti v. Everingham*, 512 Pa. 266, 516 A.2d 672

(1986), and *Bloom v. DuBois Regional Medical Center*, 409 Pa.Super. 83, 597 A.2d 671 (1991), although cited by Plaintiff, support Defendants' position. In fact, those courts dismissed the NIED counts for failure to plead the element of contemporaneous observance of traumatic infliction of injury by defendants. *See Mazzagatti*, 516 A.2d at 679 (mother who arrived at scene of accident after daughter was fatally injured by motorist not entitled to recover on theory of NIED); *Bloom*, 597 A.2d at 682-83 (husband who came upon wife who had attempted suicide at a psychiatric hospital had no cause of action for NIED because he did not witness defendants inflicting harm). Likewise, in *Taylor*, the parents of a patient who died during a catheterization procedure could not maintain an action for IIED because the mother was not present for the procedure and did not witness the physician's allegedly outrageous conduct. *Taylor*, 754 A.2d at 653. Accordingly, as with several of the individual claims above, even assuming *arguendo* that Plaintiff's complaint were not otherwise dismissed, the claims for intentional and negligent infliction of emotional distress (Counts V and VI) must still be dismissed.[FN35]

> FN35. We also note the independent tort of IIED has never expressly been approved by the Pennsylvania Supreme Court. *Taylor*, 754 A.2d at 653.

2. Claims Sounding in Negligence

Finally, we consider the individual causes of actions that sound in negligence. As discussed *supra* in Part VII.A.2, we hold that Apotex owed a duty of care to Plaintiff and Plaintiff's decedent, sufficient to give rise to liability against it. Therefore, while barred by preemption, Plaintiff's negligence-based claims

against Apotex are unaffected by our conclusions: (1) as to the lack of a duty of care owed to GSK, and (2) as to both Defendants regarding *Hahn*, which explicitly allows a plaintiff to pursue inadequate warning claims under a theory of negligence. *Hahn*, 673 A.2d at 891. Therefore, if this Court's conclusion as to preemption were found improper, Apotex would have to respond to each individual claim sounding in negligence.

a. Negligence (Count VII)

[20] Under Pennsylvania law, the elements of negligence are: (1) a duty recognized by law, requiring the actor to conform to a certain standard of conduct for protection of others against unreasonable risks; (2) failure to conform to the standard required; (3) a causal connection between the conduct and resulting injury; and (4) actual loss or damage resulting to interests of another. *Griggs v. BIC Corp.*, 981 F.2d 1429 (3d Cir.1992) (citing *Morena v. South Hills Health Sys.*, 501 Pa. 634, 462 A.2d 680, 684 n. 5 (1983)).

There is no dispute that Plaintiff has adequately plead the second, third and fourth elements. However, Plaintiff cannot plead negligence without the existence of a duty, which Apotex urges is lacking in this case. (Def. GSK's Mem. at 6-8; Def. Apotex's Mem. at 23-24). However, as we previously held that Apotex owed a duty of care to Plaintiff and Plaintiff's decedent, if preemption did not bar Plaintiff's entire complaint, his negligence claim against Apotex would be adequate to survive this motion to dismiss.

b. Negligence per se (Count VIII)

Defendants also contend that the negligence *per se* claim is impliedly preempted, evidenced by the fact that there is no private right of action under the FDCA. (Def. GSK's Mem. at 9; Def. Apotex's Mem. at 25). *See In re Orthopedic Bone Screw Prods. Liability Litig.*, 159 F.3d 817, 824 (3d Cir.1998) ("Congress has not created an express or implied private cause of action for violations of the FDCA.").

[21] The doctrine of negligence *per se* liability does not create an independent basis of tort liability but rather establishes, by reference to a statutory scheme, a standard of care appropriate to the underlying tort. Thus, if a plaintiff can show violation of a specific statute, this satisfies his or her burden of establishing duty and breach. Here, Plaintiff's negligence *per se* claim is premised on the alleged violation of the FDCA.

As discussed *supra* in Part VI, we hold all Plaintiff's claims, including that for negligence *per se,* are in fact barred by preemption.

c. Negligent Misrepresentation (Count IV)

Finally, Apotex urges that since it made no statements regarding efficacy and safety to the FDA, Plaintiff cannot show the required element of negligent misrepresentation that Apotex knew or should have known that certain representations were false. (Def. Apotex's Mem. at 19-20).

[22] The elements of negligent misrepresentation are as follows: (1) a misrepresentation of a material fact; (2) made under circumstances in which the party

ought to have known its falsity; (3) with an intent to induce another to act on it, and; (4) which results in injury to a party acting in justifiable reliance on the misrepresentation. *Bortz,* 729 A.2d at 561; *Gibbs,* 647 A.2d at 890.

Accepting as true Plaintiff's averments that material submitted to the FDA and the labeling itself was intentionally false and misleading to the FDA, the general public, the decedent's physician, and decedent herself, and that decedent and her physician relied on this information, Compl. at 86-91, this claim must survive. Also, it seems to this Court that even if Apotex did not make misrepresentations or material omissions to the FDA when it sought initial approval, Plaintiff's pleadings support the supposition that Apotex was also aware of an increased risk of suicide after approval and did not seek to strengthen its label. Compl. at 87-89. Accordingly, if Plaintiff's complaint were not otherwise dismissed, the Court would decline to dismiss the negligent misrepresentation claim.

d. Strict Liability (Count IX)

As discussed above, Defendants urge that *Hahn* holds that a manufacturer of drugs is not strictly liable for injury in connection with the use of prescription drugs. (Def. GSK's Mem. at 9-10; Def. GSK's Reply at 9). We need not re-visit Plaintiff's argument that *Hahn* does not apply at length; it suffices to say that as discussed *supra* in Part VII.C, we hold that *Hahn* clearly bars strict product liability claims against drug manufacturers, as well as any other failure-to-warn claim that does not sound in negligence. *Hahn,* 673 A.2d at 890.[FN36]

FN36. Even Plaintiff concedes that, on its face, *Hahn* appears to preclude his strict liability claim. (Pl's Supp. Mem. at 4).

VIII. Conclusion

For the foregoing reasons, Defendants' Motions to Dismiss (Doc. Nos. 5 and 10) will be granted. An appropriate Order follows.

ORDER

AND NOW, this 26th day of May 2006, based on the foregoing memorandum and upon consideration of the pleadings and briefs, it is hereby ORDERED that:

1. Defendants' Motions to Dismiss (Nos. 5 and 10) will be GRANTED WITH PREJUDICE.

2. The Clerk shall close this case.

E.D.Pa.,2006.
Colacicco v. Apotex, Inc.
432 F.Supp.2d 514, Prod.Liab.Rep. (CCH) P 17,480

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United States District Court,D. New Jersey.
Beth Ann MCNELLIS, on behalf of the Estate of Theodore DeAngelis, Deceased, and in her Own Right, Plaintiffs,
v.
PFIZER, INC., et al., Defendants.
No. Civ. 05-1286 JBS.

Dec. 29, 2005.

OPINION

SIMANDLE, District Judge:
This products liability case arises from the suicide death of Theodore DeAngelis on January 30, 2003. Plaintiffs, Beth Ann McNellis, on behalf of the estate of Theodore DeAngelis, deceased, and in her own right, contend that Zoloft, an antidepressant drug manufactured by Defendant Pfizer, Inc., which Theodore DeAngelis began taking shortly before he died, was responsible for his suicide. Plaintiffs contend principally that Pfizer's warnings regarding suicide as a possible adverse reaction associated with Zoloft were inadequate. Presently before the Court is the motion for summary judgment of Defendant Pfizer, Inc., in which the issue presented is whether, in the circumstance of the ongoing regulation and scrutiny of Zoloft, the Food and Drug Administration's regulation of prescription drugs under the Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301, *etseq.* ("FDCA") and federal regulations preempts Plaintiffs' state law tort claims arising from the

alleged failure to give sufficient warning of the possibility of an increased risk of suicide in depressed patients associated with this medication. For the reasons discussed below, this motion will be denied without prejudice to renewal upon completion of a limited period of discovery.

I. *BACKGROUND*

Plaintiff Beth Ann McNellis, suing individually and as executrix of the estate of her father, Theodore DeAngelis (collectively, "Plaintiffs"), claims that (1) Zoloft, a medication prescribed for Mr. DeAngelis, can and does "drive some people to their death" by suicide; (2) Pfizer, Inc. failed to adequately warn Mr. DeAngelis's physician of that purported fact; and (3) the purported failure to warn caused Mr. DeAngelis to ingest Zoloft and become more prone to the suicide which ended his life. (Compl. at ¶¶ 10, 12, 16.)

Theodore DeAngelis ("Decedent") was a sixty-four year old retiree who, in late 2002, began to feel depressed and consulted his family doctor. Mr. DeAngelis was initially prescribed Lexapro, an anti-depressant, but disliked that medication and was prescribed Zoloft instead on January 22, 2003. Six days later, Mr. DeAngelis consulted a psychiatrist, who prescribed a higher dose of Zoloft. Two days later, on January 30, 2003, Mr. DeAngelis was found dead, having taken his own life. Mr. DeAngelis apparently had no prior history of depression or suicidal tendencies, and had not previously taken anti-depressant medications before Lexapro.

Plaintiffs filed suit in Atlantic County Superior Court and the case was removed to this Court on March 4, 2005. Plaintiffs' claims against Defendant Pfizer, Inc. ("Pfizer") include allegations of defective design, N.J.S.A. 2A:58C-2, *etseq.* (Count I), failure to warn (Count II), violations of the New Jersey Consumer Fraud Act, N.J.S.A. 56:8-2, *etseq.* (Count III), and breach of express warranty (Count IV). Plaintiffs' primary contention is that Pfizer failed to adequately warn of the risk of suicidality associated with antidepressants such as Zoloft, despite the presence of the warning label which FDA had authorized to be given verbatim. Pfizer filed the instant motion for summary judgment, arguing that Plaintiffs' state law tort claims are preempted by the federal Food, Drug and Cosmetic Act and its implementing regulations. Extensive oral argument was held and shortly thereafter Plaintiffs filed a motion for an extension of time to complete discovery pursuant to Fed.R.Civ.P. 56(f). Supplemental briefing was received from both parties as to the merits and the Rule 56(f) motion to extend discovery, which have been carefully considered.

II. *DISCUSSION*

A. *Summary Judgment Standard of Review*

Summary judgment is appropriate when the materials of record "show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of

law."Fed.R.Civ.P. 56(c). A dispute is "genuine" if "the evidence is such that a reasonable jury could return a verdict for the non-moving party."*SeeAnderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). A fact is "material" only if it might affect the outcome of the suit under the applicable rule of law. *Id.* Disputes over irrelevant or unnecessary facts will not preclude a grant of summary judgment. *Id.*

In deciding whether there is a disputed issue of material fact, the court must view the evidence in favor of the non-moving party by extending any reasonable favorable inference to that party; in other words, "[T]he nonmoving party's evidence 'is to be believed, and all justifiable inferences are to be drawn in [that party's] favor." ' *Hunt v. Cromartie*, 526 U.S. 541, 552 (1999) (quoting *Liberty Lobby*, 477 U.S. at 255). The threshold inquiry is whether there are "any genuine factual issues that properly can be resolved only by a finder of fact because they may reasonably be resolved in favor of either party." *Liberty Lobby*, 477 U.S. at 250;*Brewer v. Quaker State Oil Refining Corp.*, 72 F.3d 326, 329-30 (3d Cir.1995) (citation omitted).

The moving party always bears the initial burden of showing that no genuine issue of material fact exists, regardless of which party ultimately would have the burden of persuasion at trial. *SeeCelotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986); *Country Floors v. Partnership of Gepner and Ford*, 930 F.2d 1056, 1061-63 (3d Cir.1991) (reviewing district court's grant of summary judgment in a trademark action); *Lucent*

Info. Manage. v. Lucent Tech., 986 F.Supp. 253, 257 (D.N.J.1997) (granting summary judgment in favor of telecommunications provider in trademark action), *aff'd*,186 F.3d 311 (3d Cir.1999); *Jalil v. Avdel Corp.*, 873 F.2d 701, 706 (3d Cir.1989), *cert.denied*,493 U.S. 1023 (1990). However, where the nonmoving party bears the burden of persuasion at trial, as plaintiff does in the present case, "the burden on the moving party may be discharged by 'showing'-that is, pointing out to the district court-that there is an absence of evidence to support the nonmoving party's case."*Celotex Corp.*, 477 U.S. at 325.

The non-moving party "may not rest upon the mere allegations or denials of" its pleading in order to show the existence of a genuine issue. Fed.R.Civ.P. 56(e). Plaintiff must do more than rely only "upon bare assertions, conclusory allegations or suspicions."*Gans v. Mundy*, 762 F.2d 338, 341 (3d Cir.1985), *cert.denied*,474 U.S. 1010 (1985) (citation omitted); *seeLiberty Lobby*, 477 U.S. at 249-50. Thus, if the plaintiff's evidence is a mere scintilla or is "not significantly probative," the court may grant summary judgment.*Liberty Lobby*, 477 U.S. at 249-50;*Country Floors*, 930 F.2d at 1061-62.

B. *Conflict Preemption*

The Supremacy Clause, Article VI, Clause 2, of the United States Constitution preempts any state law that conflicts with the exercise of federal power. *Fidelity Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 152-53 (1982). Federal law will override

state law under the Supremacy Clause when (1) Congress expressly preempts state law; (2) Congressional intent to preempt may be inferred from the existence of a pervasive federal regulatory scheme; or (3) state law conflicts with federal law or its purposes. *English v. General Elec. Co.*, 496 U.S. 72, 78-79 (1990). Defendant Pfizer argues that the third and final form of preemption, namely conflict preemption, is implicated here, and that the complaint must be dismissed.

"[I]f a state common-law claim directly conflicted with a federal regulation ..., or if it were impossible to comply with any such regulation without incurring liability under state common law, [conflict] pre-emption would occur."*Sprietsma v. Mercury Marine*, 537 U.S. 51, 65 (2002). Conflict preemption occurs either "where it is impossible for a private party to comply with both state and federal law" or where "under the circumstances of [a] particular case, [the challenged state law] stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress."*Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 372-73 (2000) (citing *Florida Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 142-43 (1963), and *Hines v. Davidowitz*, 312 U.S. 52, 66-67 (1941)). Federal regulations "have no less pre-emptive effect than federal statutes."*de la Cuesta*, 458 U.S. at 153. The imposition of damages under state law is a form of state action subject to preemption. *Geier v. American Honda Motor Co.*, 529 U.S. 861, 881 (2000). Where, as in the present circumstance, federal law does not directly preempt

claims for inadequate warnings upon prescription drugs, the Supreme Court has cautioned that "a court should not find pre-emption too readily in the absence of clear evidence of a conflict."*Id.* at 885.The Supreme Court has instructed that there is a presumption against conflict preemption, and that the court should presume "that the historic police power of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress."*New York Conference of Blue Cross & Blue Shield Plans v. Travelers Ins. Co.*, 514 U.S. 645, 655 (1995) (internal quotations omitted).

C. *Plaintiffs' Failure to Warn Claim (Count II)*

Defendant maintains that Plaintiffs' common law failure to warn claim is preempted by federal law because the Food and Drug Administration would consider any label suggesting that Zoloft "can and does cause suicide" "false and misleading," and therefore in direct contravention of the Food, Drug and Cosmetic Act.

1. *FDA Prescription Drug Approval Process*

By operation of federal law, the Food and Drug Administration ("FDA") occupies the field in determining the content of labeling on prescription pharmaceuticals such as Zoloft, as now discussed. The FDA's primary purpose is to protect consumers from dangerous prescription drugs and other products.*United States v. Dotterweich*, 320 U.S. 277 (1943). The FDA is charged with ensuring that

"human and veterinary drugs are safe and effective" and approving prescription medicines as such before they are sold in the United States. 21 U.S.C. § 393(b)(2)(B); § 355(d).

In order to obtain FDA approval for a prescription drug, the drug's manufacturer must file a New Drug Application ("NDA") with the FDA. 21 U.S.C. §§ 355(a), (b), (d). The FDCA requires the FDA to approve an application to market a prescription drug unless, *interalia,* (a) the application does not include adequate tests to show whether the drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling; (b) the results of clinical testing show that the drug is unsafe for use under the conditions prescribed, recommended, or suggested in the proposed labeling; (c) there is insufficient information to determine whether the drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling; (d) there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; or (e) based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particular. 21 U .S.C. §§ 355(c), (d).

FDA regulations mandate the general format and content of all sections of labels for all prescription drugs as well as the risk information each section must contain. 21 C.F.R. §§ 201.56, 201.57. The FDA sets out the product-specific labeling requirements in

an "approvable" letter the FDA sends to the manufacturer. *Id.* at § 314.110(a) ("FDA will send the applicant an approval letter if the application ... substantially meets the requirements of this part and the agency believes that it can approve the application ... if ... specific conditions (for example, certain changes in labeling) are agreed to by the applicant. The approvable letter will describe ... the conditions the applicant is asked to meet."). Final approval of the NDA is "conditioned upon the applicant incorporating the specified labeling changes exactly as directed, and upon the applicant submitting to FDA a copy of the final printed label prior to marketing."*Id.* at § 314.105(b).

If the manufacturer desires to make changes to the labeling after a drug is approved, it must generally submit a Supplemental NDA to the FDA pursuant to 21 C.F.R. § 314.70(b)(2)(v)(A). Although most labeling changes require a Supplemental NDA, a number of exceptions have been enumerated in 21 C.F.R. § 314.70(c)(6)(iii), which provides in pertinent part:

(6) The agency may designate a category of changes for the purpose of providing that, in the case of a change in such category, the holder of an approved application may commence distribution of the drug product involved upon receipt by the agency of a supplement for the change. These changes include, but are not limited to:

(iii)Changes in the labeling to accomplish any of the following:

(A) To add or strengthen a contraindication, warning, precaution, or adverse reaction;

(B) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage;

(C) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product;

(D) To delete false, misleading, or unsupported indications for use or claims for effectiveness; or

(E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.

21 C.F.R. § 314.70(c)(6)(iii). Thus, it is apparent that prior FDA approval need not be obtained, nor will a product be deemed mislabeled, if the manufacturer voluntarily or even unilaterally strengthens the approved warnings, precautions or potential adverse reactions upon the label pursuant to 21 C.F.R. § 314.70(c)(6)(iii)(A). The FDA's approved label as part of the NDA process can therefore be said to set the minimum labeling requirement, and not necessarily the ultimate label where a manufacturer improves the label to promote greater safety.

2. *The FDA's Approval of Zoloft*

On April 13, 1988, Pfizer submitted an NDA to the FDA seeking approval to market their drug, Zoloft, for the treatment of depression in adults. (Def.'s Ex. C, App. 49-52.) The FDA issued its approvable letter on September 30, 1991. (Def.'s Ex. F, App. 267-88.) The approvable letter contained "the Agency's proposal for the labeling of Zoloft," and requested that Pfizer "please use the proposed text verbatim."(*Id.* at App. 267.) The FDA-proposed labeling mentioned suicide in two locations. First, the FDA required that Pfizer include in the "Precautions" section the following language:

Suicide-The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Close supervision of high risk patients should accompany initial drug therapy. Prescriptions for Zoloft (sertraline) should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose.

(*Id.* at App. 276.) Second, in the "Adverse Reactions" section of the labeling, the FDA required that Pfizer include a "Psychiatric Disorders" subsection that listed "suicide attempt" as an "Infrequent" occurrence, and explained that "infrequent adverse events are those occurring in 1/100 to 1/1000 patients," and that "[i]t is important to emphasize that although the events reported occurred during treatment with Zoloft (sertraline), they were not necessarily caused by

it."(*Id.* at App. 284-85.) Pfizer followed the FDA's instructions and included the proposed labeling verbatim. Therefore, the FDA granted Pfizer final approval on December 30, 1991. (Def.'s Ex. G, App. 289-306.) Moreover, the FDA approved Zoloft for treatment of other ailments on five subsequent occasions and required the exact language with respect to suicide that has been required for initial approval.[FN1]

> FN1. In 1996, the FDA found Zoloft, as labeled, safe and effective for treatment of adult obsessive compulsive disorder ("OCD"). (Def .'s Ex. P, App. 800-25.) In 1997, the FDA found Zoloft, as labeled, safe and effective for treatment of panic disorder and of pediatric OCD. (Def.'s Ex. Q, App. 826-54; Def.'s Ex. R, App. 855-85.) In 1999, the FDA found Zoloft, as labeled, safe and effective for treatment of post-traumatic stress disorder ("PTSD"). (Def.'s Ex. S, App. 886-914.) On May 16, 2002, the FDA found Zoloft, as labeled, safe and effective for treatment of premenstrual dysphoric disorder. (Def.'s Ex. T, App. 915-949.) Finally, on February 7, 2003, the FDA found Zoloft, as labeled, safe and effective for treatment of social anxiety disorder. (Def.'s Ex. U, App. 950-87.) Notably, this most recent approval occurred shortly after Decedent committed suicide. The label's precaution concerning suicide remained the same throughout each successive approval.

3. *Preemption Analysis*

Defendant argues that Plaintiffs' inadequate warning claim, based on the notion that Pfizer should have provided a different, presumably stronger, warning before Decedent committed suicide on January 30, 2003, directly conflicts with the FDA's requirement

that Pfizer provide "verbatim" the language regarding suicide in the "Precautions" and "Adverse Reactions" sections of Zoloft's labeling at that time and, therefore, is preempted. In addition, Pfizer maintains that any label suggesting that Zoloft causes suicide would be considered by the FDA to be "false and misleading," and thus it would be in direct conflict with the FDCA. *See*21 U.S.C. § 355(d) (an NDA must be refused if the Secretary finds that a label is "false and misleading in any particular"). Plaintiffs allege that Pfizer was not preempted from strengthening the label regarding suicidality before the time of Mr. DeAngelis' death because Pfizer allegedly knew of an increased incidence requiring a stronger warning than the original FDA-approved version.

This Court finds no conflict to exist as a result of Pfizer's alleged inability to comply with both state and federal requirements. Defendant argues that if it had more strongly warned of an association between Zoloft and suicidality, it would have violated the FDA's order to use the FDA approved warning label language "verbatim." It should be noted that the word "verbatim" appears only in the FDA approvable letter to Pfizer, however, and not in any of the misbranding statutes or regulations. Moreover, as discussed above, the FDA's regulations at issue explicitly permit drug manufacturers to unilaterally strengthen warning labels at any time without regulatory pre-approval. *See*21 C.F.R. § 314.70(c)(6)(iii)(A). Indeed, this particular regulation was promulgated precisely to allow drug manufacturers to quickly strengthen label

warnings when evidence of new side effects are discovered. *See*30 Fed.Reg. 993 (Jan. 30, 1965).

Since 1965, the FDA's regulations have permitted a manufacturer "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction," without prior approval by the FDA. 21 C.F.R. § 314.70(c)(6)(iii)(A). In addition, a drug manufacturer may "add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage," without prior approval (21 C.F.R. § 314.70(c)(6)(iii)(B)), and "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," without prior approval. 21 C.F.R. § 314.70(c)(6)(iii)(C). These regulations require a manufacturer to issue a warning whenever there is "reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved."21 C.F.R. § 201.57(e). Thus, FDA's position regarding stronger warnings by drug manufacturers, as expressed through its own regulations, is that a manufacturer could, and should if warranted, provide stronger warnings as soon as it is evident that such a warning is appropriate.

As such, the FDCA and the FDA's regulations do not conflict with New Jersey's failure to warn law because those federal regulations merely set minimum standards with which manufacturers must comply. Indeed, this minimum standards approach is fully consistent with Congress' primary goal in enacting the FDCA, which is "to protect consumers

from dangerous products,"*United States v. Sullivan,* 332 U.S. 689, 696 (1948), as well as Congress' stated intent that the FDCA " 'must not weaken the existing laws', but on the contrary 'it must strengthen and extend that law's protection of the consumer ." ' *United States v. Dotterweich,* 320 U.S. 277 (1943).

Pfizer maintains, however, that § 314.70 gives manufacturers only temporary authority to strengthen the warning language on their labels. While the FDA's regulations do grant it the power to later disapprove a label strengthened pursuant to § 314.70, nothing in the regulation requires that the FDA take any action when a manufacturer makes a change pursuant to § 314.70(c).*See*56 Fed.Reg. 59290 (Nov. 25, 1991). If the FDA does nothing, the change remains in effect. Moreover, the FDA's ultimate power to disapprove the change does not render the manufacturer's unilateral strengthening of the label language a violation of any federal law. Instead, if the FDA exercises its power to disapprove the strengthened warning, the manufacturer simply ceases the use and distribution of the new label. 21 C.F.R. § 314.70(c)(7).

Pfizer also asserts that the FDA would have regarded any unilateral label change to be "false and misleading" and thus in direct conflict with 21 U.S.C. § 355(c) by pointing to the FDA's frequent reapproval of Zoloft without any changes to its warnings or its labels both before and after Decedent committed suicide. The record reflects that the FDA comprehensively evaluated Zoloft clinical-trial data

before it first found the medication safe and effective as labeled and approved it for marketing in 1991. (Def.'s Ex. C, App. 49-52; Def.'s Ex. D, App. 53-135; Def.'s Ex. G, App. 289-306; Def.'s Ex H., App. 307-65.) In addition, the FDA found Zoloft safe and effective as labeled six more times before and after January 2003. (Def.'s Ex. P., App. 800-25; Def.'s Ex. Q, App. 826-54; Def.'s Ex. R, App. 855-85; Def.'s Ex. S, App. 886-914; Def.'s Ex. T, App. 915-49; Def.'s Ex. U, App. 950-87.) In 1996, Thomas P. Laughren, M.D. of the FDA's Center for Drug Evaluation and Research submitted a detailed memo, concluding that the data presented in response to a concern about the possibility of a signal of emergent suicidality associated with sertraline use in adult and pediatric patients did not "represent a signal of risk for suicidality for either adults or children."(Def.'s Ex. X, App. 1054.) In June 2003, the FDA completed an analysis of Zoloft adverse event reports under the Best Pharmaceuticals for Children Act, including reports of suicidal ideation or behavior temporally associated with the use of Zoloft, (Def.'s Ex. KK, App. 1180-1202), and concluded that the data "do not provide any safety signals that indicate that the agency needs to do anything except continue to actively assess the evolving benefit-risk profile of these products."(Def.'s Ex. LL, App. 1203.) It was not until October of 2004, more than a year after Decedent's death, however, that the FDA "directed manufacturers of all antidepressant drugs to revise the labeling for their products to include a boxed warning and expanded warning statements that alert health care providers to an increased risk of suicidality (suicidal thinking

and behavior) in children and adolescents being treated with these agents...." (Def.'s Ex. EE, App. 1091.) No such expanded warning statements were required by FDA for the adult users of antidepressants.

This record evidence, however, at this early stage of the case, cannot suffice to satisfy Defendant's burden on the instant motion for summary judgment. Pfizer's assertion here fails to recognize that "FDA regulations are generally minimum standards of conduct" unless Congress has expressed clear intent to preempt state common law, which it has not done here. *Hill v. Searle Laboratories,* 884 F.2d 1064, 1068 (8th Cir.1989). Rather than acting as an absolute edict on the appropriate label language, the reapprovals merely confirmed the minimum labeling required and do not prove that a label strengthened pursuant to § 314.70(c)(6)(iii)(A) would be considered "false and misleading," rendering it in conflict with 21 U.S.C. § 355(e).

In further support of its argument that Plaintiffs' state law claims are preempted by federal law, Defendant offers the amicus brief filed by the United States in support of Defendant's position in *Motus v. Pfizer,* 358 F.3d 659 (9th Cir.2004).[FN2] (*See* Def.'s Ex. B, App. 17-48.) In *Motus v. Pfizer,* 127 F.Supp.2d 1085 (C.D.Cal.2000), the plaintiff claimed that Zoloft caused her husband to commit suicide. Defendant Pfizer moved for summary judgment on the grounds that the plaintiff's failure to warn claims were preempted by federal law. On appeal, the United

States, through its amicus brief, urged that the warning of a causal relation between Zoloft and suicide would have "misbranded" the drug. (Def.'s Ex. B, App. 38-43.) The United States specifically stated that

> FN2. The district court in *Motus* granted summary judgment in favor of Defendant Pfizer on the grounds that the plaintiff there had no evidence of causation. *Motus v. Pfizer, Inc.*, 196 F.Supp.2d 984 (2001). That decision was affirmed by the Ninth Circuit, but the court did "not reach the pre-emption issues raised by Pfizer on cross-appeal."*Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir.2004). Thus, the Ninth Circuit did not actually rely upon the amicus brief in deciding the appeal on other grounds.

any warning, no matter how worded, that could reasonably have been read as describing or alluding to such a relation would have been false or misleading, and therefore in conflict with federal law because there was no (and still is not) scientific support for such a warning. This is not just because FDA had rejected any link between Zoloft and suicide when, in 1991, the agency approved the drug as a treatment for depression. Subsequently, in response to petitions making similar allegations as to the related drug, Prozac, FDA found *no* link between *antidepressants* and suicide.
(*Id.* at App. 42-43) (emphasis in original) (internal citations omitted).

After oral argument, the Defendant submitted for this Court's consideration, the *amicus* brief field by the

United States on September 15, 2005, in *Kallas v. Pfizer, Inc.*, No. 2:04-CV-0998 (PGC), in the U.S. District Court for the District of Utah. The *amicus* brief in *Kallas* was submitted to the Utah court at the request of Judge Paul G. Cassell, and it was followed by a corrected *amicus* brief on September 30, 2005. The brief asserted the Government's position that "the state tort law claims in this case-under which plaintiffs argue that defendant Pfizer should be liable for using only the labeling for Zoloft approved by FDA-are preempted because they would punish Pfizer for not using a label that, as of November 2002, would have misbranded the drug."(*KallasAmicus* Br. at 2.) The brief recited in detail why, in FDA's judgment, there was not reasonable evidence of an association between Zoloft and an increased risk of suicide or suicidality as of November, 2002. *Id.* at 2-3, 12-23.The brief noted that especially intensive evaluations of the data were undertaken by FDA and manufacturers of the SSRI class of antidepressants to which Zoloft belongs, focusing on the impacts of antidepressants on pediatric and adolescent patients, beginning with the FDA's July 2003 data requests, resulting in the requirement on March 22, 2004, that Zoloft and the other SSRI medications include an enhanced warning statement recommending "close observation of adult and pediatric patients treated with those drugs for worsening of depression or the emergence of suicidality."(*Id.* at 21,*quoting* FDA Public Health Advisory "Worsening Depression and Suicidality in Patients being Treated with Antidepressant Medications," dated March 22, 2004.) The *amicus* brief summarized the FDA's conclusions

in 2002, 2003 and early 2004 that there was not reasonable evidence of an association between Zoloft (or SSRI's generally) and an increased risk of suicidality, and that suicidality had not emerged as a matter of concern based on those reviews. (*Id.* at 35-37.)

Plaintiff responded that material facts are in dispute whether, prior to Decedent's death in January, 2003, there was "reasonable evidence of an association of a serious hazard with a drug [for which] a causal relationship need not have been proved," within the meaning of 21 C.F.R. § 201.57(e), *supra*.Plaintiffs posit that the data requested by FDA from manufactures on July 22, 2003, collected over the course of years, and supports the notion that there was a link between Zoloft and suicidality prior to January, 2003, at least among the pediatric patients studied. Plaintiffs also cite to a 2000 study published by the *British Journal of Psychiatry* by Stuart Donovan, *etal.*, titled "Deliberate Self-harm and Antidepressant Drugs," pointing to a significantly elevated risk of self-harm among SSRI patients (including Zoloft users) compared with the tricyclic class of antidepressants (TCA). The enhanced incidence of suicidality in clinical trials of SSRIs associated with patients treated for anxiety and depression was also reported, according to Plaintiffs, in August 2002's "Clinical Psychiatry News," in which Dr. Arif Khan was reported to conclude that from 1985 until 2000, the rate of suicides in trials for antidepressant drugs was 718/100,000 compared to 11/100,000 in the general population. Plaintiffs also

presented the Declaration of Dr. Arvin Shroff, who retired in 2002 from the FDA, most recently as Deputy Director in the Office of Enforcement. (Pl.'s Letter Br. dated 10/21/2005 at Ex. H.) Dr. Shroff stated that in his FDA experience he does "not know of any case where FDA has considered a product to be 'misbranded' because if had a stricter warning on the label than FDA had originally approved.... Normally FDA has considered a drug 'misbranded' when a manufacturer promotes the drug for indications that are outside of the labeling."(*Id.* at ¶ 14.)Dr. Shroff's testimony is consistent with Judge Rosenbaum's opinion in *Witczak v. Pfizer, Inc.*, 377 F.Supp.2d 726, 729 (D.Minn.2005), regarding the FDA's permissiveness toward voluntary strengthening of warning labels:

The FDA's regulations do grant it the power to later disapprove a label strengthened pursuant to § 314.70. 21 C.F.R. § 314.70(c)(7). But the regulation "does not require that FDA take any action when a manufacturer" makes a change pursuant to [§ 314.70(c)]; if the FDA does nothing, the change remains in effect. *See*56 Fed.Reg. 59290 (Nov. 25, 1991). Further, even if exercised, the power to disapprove does not retroactively make the manufacturer's strengthened label a violation of any law. Rather, if the FDA exercises its power to disapprove, the manufacturer simply stops distributing the new label. 21 C.F.R. § 314.70(c)(7).

Under certain situations, the FDA's position is entitled, under Supreme Court precedent, to some

deference. In *Geier v. American Honda Motor Co.*, for example, the Supreme Court placed considerable weight upon the Department of Transportation's interpretation of the regulation at issue's objectives and its conclusion that tort suits such as the one presented would stand as an obstacle to the accomplishment and execution of those objectives. 529 U.S. at 883. The Court acknowledged that "[t]he agency is likely to have a thorough understanding of its own regulation and its objectives and is 'uniquely qualified' to comprehend the likely impact of state requirements."*Id.* (quoting *Medtronic*, 518 U.S. at 496).*SeealsoSprietsma*, 537 U.S. at 67-68 (affording deference to the agency's position on preemption). That deference may be particularly appropriate when the regulatory scheme is silent as to preemption. "[W]hen a statute speaks clearly to the issue at hand, courts 'must give effect to the unambiguously expressed intent of Congress,' but when the statute 'is silent or ambiguous,' courts must defer to a reasonable construction by the agency charged with its implementation."*Barnhard v. Thomas*, 540 U.S. 20, 26 (2003) (quoting *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 843 (1984)).

This Court, however, declines to treat statements from the *amicus* legal briefs as declarations to be afforded the preemptive force of law. Notably, the propositions Pfizer cites from the *Motus* brief were not even addressed by the *Motus* court itself. *SeeMotus*, 358 F.3d at 661. The FDA was not a party nor did the Court adopt its legal position. Moreover,

the premise of the brief's argument that Pfizer should be insulated from liability because the FDA rejected suicide warnings on the Zoloft label previously is no longer valid. In recommending labeling changes that reflect concerns about the association between SSRIs and suicidality, neither the FDA nor Pfizer can now claim, as they had in *Motus,* that no scientific basis exists for a suicide warning.

It must be noted that the issue before this Court is not one of express preemption, as presented in those cases addressing the language set forth explicitly by Congress in the Medical Device Amendments ("MDA") of 1976 to the FDCA. *See,e.g.,Medtronic, Inc. v. Lohr,* 518 U.S. 470 (1996). Indeed, the MDA's express preemption provision is considerably broader than the limiting principles of the conflict preemption doctrine in that it preempts not only when a state law actually conflicts with federal law, but even when a state law is merely "different from, or in addition to," an MDA requirement applicable to the medical device at issue. 21 U.S.C. § 360k(a). Congress did not extend such preemptive force to the regulation of pharmaceutical drugs in the FDCA.

The express preemption language of the MDA thus demonstrates that where Congress means to explicitly preempt the laws of the various states, it knows how to do so. Absent such language in the FDCA with respect to the labeling of prescription drugs, this Court's inquiry is a far narrower one, as it is limited to whether Plaintiffs' claim "would 'stand as an obstacle to the accomplishment and execution of

the objective of the safety and effectiveness" of the drug specifically and "would conflict with the federal requirements imposed" by the FDCA. *Horn v. Thoratec Corp.*, 376 F.3d 163, 179 (3d Cir.2004) (quoting *Geier*, 529 U.S. at 873). This Court is unwilling to find, as Pfizer would have it, that Congress intended to obviate the very state laws that provide remedies to consumers harmed by dangerous products and deceptive marketing in the absence of a clear and compelling Congressional statement. *SeeBates v.. Dow Agrosciences LLC*, 125 S.Ct. 1788, 1802 (2005) ("If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly.").

In its argument that conflict preemption applies in this case, Pfizer places significant weight on the Third Circuit's decision in *Horn v. Thoratec Corp.*, 376 F.3d 163 (3d Cir.2004). In *Horn*, the Third Circuit stated that the state tort law claims were in "severe tension" with the federal requirement regarding medical devices. *Id.* at 177.The court in *Horn*, however, was interpreting the express preemption clause of the MDA, which commands: "No State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement-(1) which is different from, *or in addition to*, any requirement applicable to this chapter to the device."21 U.S.C. § 360k(a) (emphasis added); *Horn*, 376 F.3d at 166. Thus, by this provision, Congress has clearly expressed its intent that stricter state law requirements should not

be permitted in the case of medical devices. The opposite, however, is true with prescription drugs, as discussed above. In the realm of prescription drugs regulated by the FDA under the FDCA, this Court finds that the federal labeling requirements are minimum standards; states can impose stricter requirements regarding labeling and warnings if they so choose by operation of customary tort law. The only limiting regulation is that the warnings must not be false or misleading, as that would lead ultimately to the FDA's rejection of Pfizer's labeling, and that any requirement for stricter labeling be based upon at least reasonable evidence of the association of a serious hazard with the drug, even if a causal relationship has not been proved, consistent with 21 C.F.R. § 201.57(e). Here, the question of whether the FDA would have so acted can only be answered when it is clear what Pfizer knew about the link between Zoloft and suicidality, whether (as Plaintiffs allege) the company withheld crucial information on that issue from the FDA in seeking approval and reapproval of the drug, and how, if at all, its withholding of any relevant information matters.

Thus, stated differently, if Plaintiffs can demonstrate that Pfizer had knowledge of a heightened risk of suicidality, which should have resulted in enhanced labeling beyond the FDA-approved warning, then the FDCA does not preempt Plaintiffs' claim. If Plaintiffs can prove to the factfinder that Pfizer had, prior to January 2003, "reasonable evidence of an association of a serious hazard [suicidality] with a drug [Zoloft or the SSRI class generally,]" *see* 21 C.F.R. § 201.57(e),

then the enhanced warning sought by Plaintiffs herein would not be preempted by the FDCA. There remains, at this early stage, the need for Plaintiffs to have the opportunity to obtain discovery upon this material issue before Plaintiffs can fairly be called upon to rebut Pfizer's showing on summary judgment, as requested by Plaintiffs in their Rule 56(f) motion. At this stage, therefore, summary judgment will be denied without prejudice.

D. *Plaintiffs' Defective Design, Warranty and Consumer-Fraud Claims*

In addition to their failure to warn claim, Plaintiffs assert claims for defective design under N.J.S.A. 2A:58C-2, *etseq*. (Count I); violation of the New Jersey Consumer Fraud Act, N.J.S.A. 56:8-2, *etseq*. (Count III); and breach of express warranty (Count IV). At oral argument, Plaintiffs' counsel clarified that the Complaint does not allege that the product was defective or adulterated when consumed by Mr. DeAngelis, as the essential basis of liability was the content of labeling and warnings. These additional claims are also not preempted for the reasons set forth above because they, like Plaintiffs' inadequate warning claim, present no conflict between federal and state law arising solely from the approved labeling of this pharmaceutical. While these claims may present Plaintiffs with an especially steep burden in the context of this case, this Court cannot agree with Pfizer that Congress implied that preemption of such claims without a more specific indication of congressional intent.

E. *Plaintiffs' Rule 56(f) Motion*

By agreement of the parties, no discovery has been exchanged in this case. After oral argument was heard in this case, Plaintiffs filed a motion for an extension of time to complete discovery pursuant to Rule 56(f), Fed.R.Civ.P. Rule56(f) provides in pertinent part that

Should it appear from the affidavits of a party opposing the motion that the party cannot for reasons stated present by affidavit facts essential to justify the party's opposition, the court may refuse the application for judgment or may order a continuance to permit affidavits to be obtained or depositions to be taken or discovery to be had or may make such other order as is just.

Defendant's summary judgment motion and extensive affidavits and appendices in support were filed on May 10, 2005. Thereafter, Plaintiffs agreed by Consent Order filed May 27, 2005 to Defendant Pfizer's request for a stay of discovery while the legal issue of conflict preemption was decided. Now, however, Plaintiffs argue that while . it was anticipated that the law, and not the factual record, would be the deciding factor in this Court's determination of the conflict preemption issue, it is clear that the factual record may have more relevance. (Rule 56(f) Affidavit of Gregory Spizer at ¶ 7.) What Pfizer knew and when it knew it, Plaintiffs

maintain, can only be obtained through the Defendant during discovery. (*Id.* at ¶ 8.)

"[W]here the facts are in possession of the moving party a continuance of a motion for summary judgment for purposes of discovery should be granted almost as a matter of course."*Miller v. Beneficial Mgmt. Corp.*, 977 F.2d 834, 846 (3d Cir.1992) (holding in certain circumstances the incomplete state of discovery itself warrants preclusion of summary judgment on the merits) (quoting *Sames v. Gable*, 732 F.2d 49, 51 (3d Cir.1984)). Here, Defendant alone is in possession of all relevant information. The studies Pfizer performed on Zoloft, the risks inherent from use of the drug, including suicidal ideation, adverse event reports related to Zoloft use, the manner in which Zoloft was sold and marketed to physicians and patients, and the communications it had with the FDA about all of these topics are all relevant to Plaintiffs' arguments.

This Court will therefore grant Plaintiffs' Rule 56(f) motion and permit a 120 day period of discovery, at the conclusion of which, Plaintiffs should be prepared to submit a competent expert report [FN3] to support its argument that there exists a prima facie basis for believing that Pfizer possessed sufficient information before January, 2003 from which it is reasonable to conclude there existed a link between Zoloft and enhanced suicidality which rendered the product warning inadequate. This period enables Plaintiffs, through prompt efforts, to seek and obtain relevant discovery within the scope of this motion, focusing on

the evidence of suicidality prior to the Decedent's death in January, 2003. The period is not so lengthy, however, that Plaintiffs can embark upon a fishing expedition in hopes of obtaining something of interest.[FN4]Until Plaintiffs have this opportunity to obtain relevant discovery, the present summary judgment motion is premature.

FN3. In matters of epidemiology such as the evaluation of adverse reactions to prescription medication, such an association can only be shown through the testimony of a competent expert using reliable methodology as required by Rule 702, Fed.R.Evid. *See,e.g.,DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.3d 941, 954 (3d Cir.1990). Here, of course, the scope of the expert's task is two-fold; first, to identify whether evidence supports a statistically significant elevation of the risk of suicidality in Zoloft (or SSRI class drugs) in depressed patients, and second, whether it is probable, to a reasonable medical probability, that ingestion of Zoloft was a proximate cause of Mr. DeAgelis' suicide. In the Third Circuit, the latter aspect may also be demonstrated by a "thorough differential diagnosis" by a medical expert who is able to reliably rule out other causes of plaintiff's death, *see,e.g.,Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 151 (3d Cir.1999).

FN4. The Court is cognizant that at oral argument Plaintiffs' counsel admitted he was in possession of no facts demonstrating that Pfizer actually understated the risk of suicidality, but counsel believes such information will be developed in discovery.

III. *CONCLUSION*

For the reasons discussed above, Defendant's motion for summary judgment will be denied without

prejudice and Plaintiffs' motion pursuant to Fed.R.Civ.P. 56(f) will be granted, and relevant discovery within the scope of this summary judgment motion may be exchanged promptly; Plaintiffs, as the parties opposing this summary judgment motion, must serve a competent expert's report within 120 days demonstrating a basis for prevailing upon its claims on all counts, alleging deficient warnings and causation and especially with regard to an analysis of data showing that the risk of suicidality as of January, 2003, associated with Zoloft was not adequately reflected on the FDA-approved label. If Plaintiffs are unable to do so, Pfizer may renew this summary judgment motion. The accompanying Order is entered.

ORDER

This matter having come before the Court upon the motion of Defendant Pfizer, Inc. for summary judgment as well as the motion of Plaintiffs Beth Ann McNellis, on behalf of the Estate of Theodore DeAngelis, deceased, and in her own right, for an extension of time to complete discovery pursuant to Fed.R.Civ.P. 56(f); and the Court having considered the submissions of the parties in support thereof and in opposition thereto; and the Court having heard oral argument on July 6, 2005; and for the reasons set forth in the Opinion of today's date; and for good cause shown;

IT IS this *29th* day of December, 2005 hereby

ORDERED that Defendant Pfizer, Inc.'s motion for summary judgment [Docket Item No. 12-1] shall be, and it hereby is, *DENIED WITHOUT PREJUDICE;*

IT IS FURTHER ORDERED that Plaintiffs' motion for an extension of time to complete discovery pursuant to Fed.R.Civ.P. 56(f) [Docket Item No. 24-1] shall be, and it hereby is, *GRANTED;* and

IT IS FURTHER ORDERED that Plaintiffs may seek relevant discovery within the scope of this motion, to be concluded within the next 120 days, at which time Plaintiffs shall be required to serve a competent expert's report analyzing the data regarding suicidality and demonstrating prima facie why the Defendant's failure to supplement the FDA-approved label for Zoloft, as of January, 2003, is actionable in this case and how such conduct by Defendant resulted in an inadequate warning that was more likely than not a probable cause of Decedent's suicide.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

Civil No. 05-1286 (JBS)

BETH ANN McNELLIS, on behalf
of the Estate of Theodore
DeAngelis, Deceased, and IN
HER OWN RIGHT,
Plaintiffs,

v.

PFIZER, INC., et al.,
Defendants.

HONORABLE JEROME B. SIMANDLE

ORDER

This matter having come before the Court upon the motions of Defendant Pfizer, Inc. (1) to vacate this Court's December 29, 2005 Order and enter summary judgment in favor of Defendant, or in the alternative (2) to certify the Order for immediate interlocutory appeal; and the Court having considered the

submissions fo the parties in support thereof and in opposition thereto; and the Court having heard oral argument on June 30, 2006; and for the reasons set forth in the Opinion of today's date; and for good cause shown;

IT IS this **29th** day of September, 2006 hereby

ORDERED that Defendant Pfizer, Inc.'s motion to vacate this Court's December 29, 2005 Order and enter summary judgment in favor of Defendant (Docket Item No. 30) shall be, and it hereby is , **DENIED**;

IT IS FURTHER ORDERED that Defendant Pfizer's moiton, pursuant to 28 U.S.C. § 1292(b), to certify this Court's December 29, 2005 Order for interlocutory appeal shall be, and it hereby is, **GRANTED**, and the Court certifies the following question as a controlling question of law as to which

there is a substantial ground for difference of opinion and as to which an immediate appeal may materially advance the ultimate termination of the litigation;

> Whether that the United States Food and Drug Administration's requirements for the form and content of the labeling for the prescription antidepressant Zoloft preempted New Jersey's failure-to-warn law, under the doctrine of conflict preemption, where the FDA's regulations at 21 C.F.R. 201.57(d) and 314.70(c)(6)(iii) permit a manufacturer to unilaterally enhance its warning when the manufacturer has reasonable evidence of an association of a serious hazard with a drug.

IT IS FURTHER ORDERED the proceedings in this case shall be and hereby are, **STAYED** pending a determination by the Court of Appeals.

s/ Jerome B. Simandle
JEROME B. SIMANDLE
United States District Judge

United States District Court,D. New Jersey.
Beth Ann MCNELLIS, on behalf of the Estate of Theodore DeAngelis, Deceased, and In Her Own Right, Plaintiffs,
v.
PFIZER, INC., et al., Defendants.
No. Civ. 05-1286(JBS).

Sept. 29, 2006.

OPINION

SIMANDLE, District Judge:
This products liability case arises from the suicide death of Theodore DeAngelis on January 30, 2003. Plaintiffs, Beth Ann McNellis, on behalf of the estate of Theodore DeAngelis, deceased, and in her own right, bring this action contending that Zoloft, an antidepressant drug manufactured by Defendant Pfizer, Inc., ("Pfizer") which Theodore DeAngelis began taking shortly before he died, was responsible for his suicide. Plaintiffs contend principally that Pfizer's warnings regarding suicide as a possible adverse reaction associated with Zoloft were inadequate, and that Pfizer is liable for failure to warn under New Jersey Product Liability Act. In 2005, Pfizer filed a motion for summary judgment arguing that Plaintiffs' state law tort claims are preempted by the Federal Food, Drug and Cosmetic Act (the "FDCA") and its implementing regulations. On December 29, 2005, this Court issued an Opinion (the "December 29 Opinion") and Order (the

"December 29 Order") denying Pfizer's motion, without prejudice to renewal after a period of factual discovery. Presently before the Court is Pfizer's motion to vacate this Court's summary judgment order or, in the alternative, to certify under 28 U.S.C. § 1292(b) the December 29 Order for immediate interlocutory appeal. For the reasons expressed below, the Court will (1) deny Pfizer's motion to vacate this Court's December 29 Order but (2) will grant Pfizer's motion to certify the December 29 Order (as augmented by today's Order) for interlocutory appeal and, pursuant to 28 U.S.C. § 1292(b), stay the proceedings in this Court pending a determination by the Court of Appeals.

1. *BACKGROUND*

The Court will include only a brief summary of the relevant facts. Theodore DeAngelis ("DeAngelis") was a sixty-four year old retiree who, in late 2002, began to feel depressed and consulted his family doctor. Mr. DeAngelis was initially prescribed Lexapro, an anti-depressant, but disliked that medication and was prescribed Zoloft instead on January 22, 2003. Six days later, Mr. DeAngelis consulted a psychiatrist, who prescribed a higher dose of Zoloft. Two days later, on January 30, 2003, Mr. DeAngelis was found dead, having taken his own life. Mr. DeAngelis apparently had no prior history of depression or suicidal tendencies, and had not previously taken anti-depressant medications before Lexapro.

Plaintiff Beth Ann McNellis ("McNellis"), suing individually and as executrix of the estate of her father, DeAngelis,[FN1] claims that (1) Zoloft, a medication prescribed for Mr. DeAngelis, can and does "drive some people to their death" by suicide; (2) Pfizer failed to adequately warn Mr. DeAngelis's physician of risks of suicidality associated with Zoloft that had become apparent prior to his prescribing of Zoloft to Mr. DeAngelis; and (3) the purported failure-to-warn caused Mr. DeAngelis to ingest Zoloft and become more prone to the suicide which ended his life. (Compl. at ¶¶ 10, 12, 16.)

> FN1. McNellis and DeAngelis shall be referred to collectively as the "Plaintiffs."

Plaintiffs' claims against Defendant Pfizer include allegations of (1) defective design, N.J.S.A. 2A:58C-2, *etseq.* (Count I), (2) failure-to-warn (Count II), (3) violations of the New Jersey Consumer Fraud Act, N.J.S.A. 56:8-2, *etseq.* (Count III), and (4) breach of express warranty (Count IV). Plaintiffs' primary contention is that Pfizer failed to adequately warn of the risk of suicidality associated with antidepressants such as Zoloft, despite the presence of the warning label which the FDA had authorized to be given verbatim. Pfizer filed a motion for summary judgment, arguing that Plaintiffs' state law tort claims are preempted by the federal Food, Drug and Cosmetic Act and its implementing regulations. On December 29, 2005, this Court denied Pfizer's motion. *SeeMcNellis v. Pfizer, Inc.*, 2005 U.S. Dist. LEXIS 37505 (D.N.J. December 29, 2005).

This Court based its December 29, 2005 ruling in part on regulations of the Food and Drug Administration (FDA) at 21 C.F.R. § 314.70(c)(6) which, under certain circumstances, allows a pharmaceutical manufacturer to strengthen warnings while FDA approval is being sought for an enhanced warning. *Seeid.*Specifically, the Court held that "[i]f Plaintiffs can prove to the fact finder that Pfizer had, prior to January, 2003, 'reasonable evidence of an association of a serious hazard with a drug,'*see*21 C.F.R. § 201.57(e), then the enhanced warning sought by Plaintiffs herein would not be preempted by the FDCA."*Id.* at *33.

Pfizer now brings this motion (1) to vacate this Court's December 29 Order or, (2) in the alternative, to certify the December 29 Order for interlocutory appeal, and (3) for an order staying discovery pending appeal. Pfizer moves to vacate the order on the basis that new evidence exists that establishes the actual meaning and intent of 21 C.F.R. § 314.70. Pfizer cites as new evidence a document published by the Food and Drug Administration ("FDA" or the "Agency") on January 24, 2006, about a month after this Court's December 29 Opinion, titled "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" (the "Final Rule"). The Final Rule, according to Pfizer, explicitly explained the agency's purposes, policies, and intent regarding Section 314.70, how the agency precludes any deviation in labeling notwithstanding the language of Section 314.70, and why preemption should apply in cases such as the present case. *See*21

Fed.Reg. 3922, 3933-36, 3967-69 (Jan. 24, 2006). The FDA's new reading of its labeling regulations, the text of which is unchanged in relevant part, constitutes the new evidence that Pfizer posits in this motion to vacate.

II. *DISCUSSION*

A. *Pfizer's Motion to Vacate*

The district court has inherent power to vacate or revise its interlocutory orders before final judgment when justice so requires. *SeeGallant v. Telebrands Corp.*, 35 F.Supp.2d 378, 394 (D.N.J.1998). An interlocutory order, such as the prior order herein denying summary judgment, may be vacated when there is newly discovered, non-cumulative evidence or in light of relevant changes in the facts or law of a case that would have altered earlier rulings by the Court. *Seeid.;seealsoElectric Mobility Corp. v. Bourns*, 87 F.Supp.2d 394, 401 (D.N.J.2000)("Reconsideration may be justified on the basis of an intervening change in law ... and is not necessarily barred by Local Civ. R. 7.1(g), requiring motions for reconsideration to be filed within ten days of an order.") Such a motion to vacate, however, is not intended as a vehicle to re-litigate issues that have already been decided. *SeeGallant*, 35 F.Supp.2d at 394. Rather, "[i]n the absence of newly discovered, non-cumulative evidence, the parties should not be permitted to reargue previous rulings made in the case."*Id.*

1. The Preamble to the Final Rule is New Evidence

In its submissions and at oral argument, Pfizer argues that there have been two significant developments since the December 29 Order which constitute new evidence and that this new evidence should cause the Court to reconsider its denial of Pfizer's earlier motion for summary judgment. The most significant development, Pfizer argues, is the issuance of the Final Rule on January of 2006. The preamble to the Final Rule (the "Preamble"), according to Pfizer, constitutes new, compelling evidence requiring vacation of this Court's December 29 Order because it confirms the position the FDA had taken in amicus briefs in other cases that Pfizer had earlier submitted for consideration by this Court.[FN2]The second development is the recent decision of *Colacicco v. Apotex, Inc.*, 432 F.Supp.2d 514 (E.D.Pa.2006), in which the court (1) gave deference to the FDA's interpretation (outlined in the Preamble) of its own regulations, and (2) held that the regulations to the FDCA preempt state failure-to-warn tort claims.

> FN2. Specifically, Pfizer submitted amicus briefs from the *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir.2004) (the "*Motus* brief") and *Kallas v. Pfizer, Inc.*, No. 2:04-CV-0998 (Utah September 15, 2005)(the "*Kallas* brief"). Each of these briefs was considered herein previously and they are not "new."

Plaintiffs counter-argue that Pfizer's motion to vacate rests on a faulty premise-that the Preamble to the FDA's newly issued Final Rule constitutes new

evidence. According to Plaintiffs, the Preamble simply repeats the same position that was already argued to and rejected by this Court. Plaintiffs point out numerous examples of where both Pfizer and the Court have explained that the issue before the Court on Pfizer's motion for summary judgment was whether the FDCA and the FDA's regulations conflict with New Jersey's failure-to-warn law and whether the state law cause of action is preempted. Now, according to Plaintiffs, Pfizer seeks the "unusual" relief of a motion to vacate because the FDA's position on the preemptive effect of its regulations-which is identical to the FDA's position as articulated in the *Motus* and *Kallas* amicus briefs-is now articulated in "an advisory preamble" to the Final Rule. (Pl.'s Opp. Br. at 5.) Plaintiffs continue, contending that the format for this advisory opinion is meaningless because the Preamble and the *Motus* and *Kallas* amicus briefs carry the same weight-they are both advisory positions from the FDA, *see*21 C.F.R. § 10.80, and, thus, there is no new evidence before the Court. *SeeGallant,* 35 F.Supp.2d at 378.

This Court disagrees with Plaintiffs and finds that the Preamble to the Final Rule is new evidence that should be considered in a motion to vacate. The Preamble is an official agency statement purporting to establish preemption of conflicting state law claims. At minimum, the Final Rule is an advisory opinion representing the formal position of the FDA. As an advisory opinion, it "represents the formal position of FDA on a matter and except [under unusual situations involving an immediate or

significant danger to health], obligates the agency to follow it until it is amended or revoked."21 C.F.R. § 10.85(e). The Preamble is also distinguishable from an amicus brief. Amicus briefs, by their nature, are drafted in the context of specific ongoing litigation. The *Motus* and *Kallas* briefs, for example, represent the FDA's position on an issue that is tailored to those particular cases. In contrast, in the Preamble, the Agency (1) put forth its general position on the preemptive effect of its regulations (rather than a position tailored to a particular case) and (2) is obligated to follow it until amended or revoked. *See*21 C.F.R. § 10.85(e).

2. Although the Issuance of the Preamble is "New Evidence," it does not Warrant Vacation of this Court's December 29 Order

a. Pfizer's Argument

Next Pfizer argues that the issuance of the Final Rule articulating the FDA's interpretation of its regulations (specifically, that the regulations preempt state tort law) requires this Court to vacate its December 29 Order. According to Pfizer, because the Preamble represents an administrative agency interpreting its own regulations, the FDA's interpretation of regulations related to the FDCA are entitled to substantial deference. *SeeAuer v. Robbins,* 519 U.S. 452, 117 S.Ct. 905, 137 L.Ed.2d 79 (1997)(courts must give an administrative agency's interpretation of its own regulations substantial deference). Specifically, Pfizer argues that, in the

Preamble, the FDA reaffirms that "under existing preemption principles, FDA approval of labeling ... preempts conflicting or contrary State law."71 Fed.Reg. at 3934. The Preamble to the Final Rule also addresses the factual situation where the FDA has specifically considered and rejected the warning a plaintiff advocates, and explains why such an action by a plaintiff would, if allowed to proceed, impair the Agency's safety purposes and policies. *Id.* Specifically, the Preamble states:

FDA believes that State laws conflict with and stand as an obstacle to achievement of the full objectives and purposes of Federal law when they purport to compel a firm to include in labeling or advertising a statement that FDA has considered and found scientifically unsubstantiated.

Id. at 3935.Pfizer argues that this statement explains why two positions that served as the basis for this Court's December 29 Order misinterpret the agency's regulations. First, the FDA states that its labeling regulations are not "minimum standards" (as the Court's Opinion holds) but "establish both a 'floor' and 'ceiling.' "*Id.* Second, the FDA states that Section 314.70-the FDA regulation that explicitly permits drug manufacturers to unilaterally strengthen warning labels at any time without regulatory pre-approval-negates the preemptive effect of labeling requirements and "conflicts with the agency's own interpretations" of its own regulations. *Id.* Rather, the FDA explains that Section 314.70 does not preclude preemption because the FDA remains the final

arbiter of the form and content of all labeling regardless of whether the manufacturer may temporarily alter a medication's label.

Next Pfizer argues that the Final Rule also addresses why preemption precludes a plaintiff from arguing to a jury or court that a manufacturer withheld information from the FDA. The Preamble to the Final Rule states that the FDA precludes:

[C]laims that a drug sponsor breached an obligation to warn by failing to include a statement in labeling or in advertising, the substance of which has been proposed to FDA for inclusion in labeling, if that statement was not required by FDA at the time plaintiff claims the sponsor had an obligation to warn (unless FDA has made a finding that the sponsor withheld material information relating to the proposed warning before plaintiff claims the sponsor had the obligation to warn.)

21 Fed.Reg. at 3936;*seeBuckman Co. v. Plaintiff's Legal Comm.*, 531 U.S. 341, 352-53, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001) ("fraud on the FDA" theories are preempted by federal law); *Garcia v. Wyeth-Ayerst Labs.*, 385 F.3d 961, 966 (6th Cir.2004) (affirming district court decision finding preemption because "*Buckman* teaches that state tort remedies requiring proof of fraud committed against the FDA are foreclosed since federal law preempts such claims.")

The FDCA contains no explicit preemption of state law as to labeling of pharmaceutical drugs, as Congress has historically declined to take this step.[FN3] If the FDCA is seen as preempting state tort claims for failure to warn, it is only through conflict preemption that this can occur. Absent such language, this Court's inquiry is limited to whether Plaintiffs' claim "would stand as an obstacle to the accomplishment and execution of the objective of the safety and effectiveness" of the drug specifically and "would conflict with the · federal requirements imposed' by the FDCA." *Horn v. Thoratec Corp.*, 376 F.3d 163, 179 (3d Cir.2004) (internal quotations omitted).

> FN3. In contrast, the Medical Devices Amendment of 1976 to the FDCA contains an express preemption provision that is considerably broader than the limiting principle of the conflict preemption doctrine in that it "preempts not only when a state law actually conflicts with federal law, but even when a state law is merely 'different from, or in addition to,' [a Medical Devices Amendment] requirement applicable to the medical device at issue."*McNellis*, 2005 U.S. Dist. LEXIS at *30 (citing 21 U.S.C. § 360k(a)).

This Court must be mindful that the Supreme Court has instructed that there is a presumption against conflict preemption, and that the Court should presume "that the historic police power of the States were not to be superceded by the Federal Acts unless that was the clear and manifest purpose of

Congress."*New York Conference of Blue Cross & Blue Shield Plans v. Travelers Ins. Co.*, 514 U.S. 645, 655, 115 S.Ct. 1671, 131 L.Ed.2d 695 (1995) (internal quotations omitted). With this in mind, this Court finds that, despite the issuance of the Preamble in January of 2006, vacation of the Court's December 29 Order is not warranted for two reasons. First, the text of the regulatory language upon which this Court seized in rejecting Pfizer's preemption argument (i.e., that a drug manufacturer is permitted to unilaterally strengthen the warnings on its labels under certain circumstances) was not changed in the Final Rule amendments. Indeed, the text of the relevant FDA regulations has been unchanged for years. As such, there can be no conflict preemption because the FDA's regulations do not conflict with New Jersey's failure-to-warn laws. Second, while the Court's deference to the agency's interpretation is substantial, it is not dispositive of the issue because (1) the FDA's position regarding the preemptive force of its regulations has not been consistent, requiring this Court to give it less deference, (2) the regulations at issue empower drug manufacturers to enhance the labeling warnings beyond the approved text when new risks emerge (otherwise, these regulations would have no meaning at all), and (3) as this Court explained in its December 29 Opinion, this Court finds certain of the cases Pfizer relies on in support of their argument unpersuasive, as they interpret medical device labeling regulations that contain an express preemption clause, while the Food, Drug and Cosmetic Act does not.

1. The FDA's Final Rule Does Not Conflict with New Jersey's Failure-to-Warn Law

In its December 29 Opinion, this Court found that no conflict existed as a result of Pfizer's alleged inability to comply with both state and federal requirements. *McNellis,* 2006 U.S. Dist. LEXIS at *16-17. In making this conclusion, the Court noted that the FDA's regulations at issue "explicitly permit drug manufacturers to unilaterally strengthen warning labels at any time without regulatory pre-approval." *Id.* at *17 (citing 21 C.F.R. § 314.70(c)(6)(iii)(A)). Moreover, when discussing FDA regulations that permit a drug manufacturer to "add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage" or "add or strengthen an instruction about dosage or administration that is intended to increase the safe use of the drug product" without prior approval, *see* 21 C.F.R. § 314.70(c)(6)(iii)(B)-(C), this Court held that "[t]hese regulations require a manufacturer to issue a warning whenever there is 'reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved.'" *Id.* at *17 (citing 21 C.F.R. § 201.57(e)). The Court concluded that "the FDCA and the FDA's regulations do not conflict with New Jersey's failure-to-warn law because those federal regulations merely set minimum standards with which manufacturers must comply." *Id.* at *18.

Here, vacation of this Court's December 29 Order is not warranted because the regulatory language seized

upon by the Court in rejecting Pfizer's preemption arguments (*see*21 C.F.R. § 201.57(e) and 314.70(c)(6)) is unaffected by the rule amendments articulated in the Final Rule. FDA regulations explicitly allow a manufacturer to add or strengthen warnings without prior FDA approval. *See*21 C.F.R. § 314.70(c)(6)(iii)(A). Indeed, the amended version of 21 C.F.R. § 201.57(e) (which will be recodified as 21 C.F.R. § 201.80(e)) will still place an affirmative responsibility upon drug manufacturers to revise a drug's label to "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved."21 C.F.R. § 201.57(e)). As such, the FDA's approved warnings will continue to reflect merely "minimum standards," to be enhanced as soon as new evidence of a serious hazard exists, whether or not a causal relationship is proved. To the extent that the Preamble purports to forbid a manufacturer from enhancing the warning when reasonable evidence of an association of a serious hazard emerges, the Preamble is squarely contradicted by the plain language of the regulations themselves, namely, 21 C.F.R. § 314.70(c)(6)(iii)(A) and 21 C.F.R. § 201.57(e).

The Preamble's words are irreconcilable tension with the Final Rule itself. Specifically, the Final Rule states:

While a sponsor is permitted to add risk information to the [full prescribing information] without first obtaining FDA approval via a [change being effected] supplement, FDA reviews all such submission and

may later deny approval of the supplement, and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading under Section 502(a) of the Act.

71 Fed.Reg. at 3934. Thus, despite the issuance of the Final Rule and the language existing in the Preamble, the rationale of the Court's December 29 Opinion remains sound.

2. The Preamble Cannot be Enforced to Nullify the FDA's Own Regulations it Purports to Interpret.

As discussed previously, under the Final Rule, 21 C.F.R. § 314.70(c)(6)(iii) will still explicitly permit a drug manufacturer to change the labeling of a drug in order to "add or strengthen a contraindication, warning, precaution or adverse reaction...." Moreover, the amended version of 21 C.F.R. § 201.57(e) (now 21 C.F.R. § 201.80(e)) will still place an affirmative duty upon drug manufacturers to revise a drug's label to include a warning "as soon as there is reasonable evidence of an association of serious hazard with a drug...." If drug manufacturers were to follow the FDA's interpretation of these regulations as set out in the Preamble-which states that the FDA's labeling requirements are not "minimum standards" and that, instead, those regulations "establish both a 'floor' and a 'ceiling,' "*se e* 21 Fed.Reg. at 3934,-drug manufacturers would be precluded from enhancing a warning on their own. As such, the Preamble cannot be enforced as doing so would nullify Section 314.70(c)(6)(iii) and Section 201.57(e). An agency's

interpretation of its own regulations which would nullify those regulations is not entitled to controlling weight.

3. The Interpretation Set Out in the Preamble is Not Entitled to Substantial Deference Because the FDA's Position Regarding Preemption has not been Consistent.

According to Pfizer, the FDA's interpretation of its own regulation (Section 314.70) is controlling unless that interpretation is "clearly erroneous" or "inconsistent" with FDA regulations; here, Pfizer continues, the FDA's conclusion that Section 314.70 does not preclude preemption is "neither plainly erroneous nor contrary to any FDA regulation."(Def.'s Br. at 7.) Pfizer also argues that the FDA's assessment of the preemptive effect of its actions is also entitled to substantial deference. In support of this position, Pfizer cites *Medtronic, Inc. v. Lohr,* 518 U.S. 470, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996), in which the Supreme Court held that the FDA, in interpreting the express preemption provision of the Medical Devices Act (21 U.S.C. § 360(k)), "is uniquely qualified to determine whether a particular form of state law 'stands as an obstacle to the ... execution of the full purpose of objective of Congress,' and therefore, whether it should be pre-empted."518 U.S. at 496 (quoting *Hines v. Davidowitz,* 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941)). This is because the FDA has a "special understanding of the likely impact of both state and federal requirements, as well as an understanding of whether ... state requirements may

interfere with federal objectives."*Id.* at 506 (Breyer, J., concurring). The Supreme Court has ruled similarly with respect to the deference a court must give to the Department of Transportation's interpretation of its regulations. *SeeGeier v. American Honda Motor Co.*, 529 U.S. 861, 883, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000) (holding that because the underlying "subject matter is technical" and the background into the issue "complex and extensive," the Department of Transportation was "uniquely qualified to comprehend the likely impact of state requirements.") Thus, according to Pfizer, the Court should vacate its December 29 Order and grant Pfizer summary judgment because Plaintiffs' claims are preempted by the FDCA.

For the reasons next discussed, this Court, as it did in its December 29 Opinion with respect to legal positions taken by the FDA in amicus briefs, declines to give the Preamble preemptive force of law for two reasons. First, according to recent Supreme Court precedent, this Court is required to give less deference to an agency's interpretation of its own regulations if the agency's interpretation of those regulations has not been consistent. Second, this Court finds that the majority of cases cited by Pfizer in support of its argument that this Court should grant deference to the FDA's interpretation of its regulations involve the agency's interpretation of an express preemption clause. As such, these arguments carry little weight in this Court's determination of the present regulations.

(i) Inconsistency between the FDA's 2006 Preamble and the 2000 Proposed Rule

In determining the amount of deference to give to agency interpretations of their own regulations, this Court must consider whether an agency's interpretation of its own regulations has been consistent. *SeeUnited State v. Mead Corp.*, 533 U.S. 218, 228, 121 S.Ct. 2164, 150 L.Ed.2d 292 (2001) ("The fair deference to an agency administering its own statute has been understood to vary with circumstances, and courts have looked to (1) the degree of the agency's care, (2) its *consistency*, formality and relative expertness ....") (emphasis added); *seealsoGood Samaritan Hosp. v. Shalala*, 508 U.S. 402, 417, 113 S.Ct. 2151, 124 L.Ed.2d 368 (1993) ("[T]he consistency of an agency's position is a factor in assessing the weight that position is due.") The Supreme Court has affirmed this stance towards deference to the FDA's interpretation of the Public Health Services Act, *seeHillsborough County v. Automated med. Labs, Inc.*, 471 U.S. 707, 714, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985),[FN4] and more recently in the Environmental Protection Agency's interpretation of the Federal Insecticide, Fungicide, and Rodenticide Act. *SeeBates v. Dow Agrosciences, LLC*, 544 U.S. 431, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005).[FN5]

FN4. In *Hillsborough County*, when discussing the amount of deference to give to the FDA's interpretation of the FDA's blood plasma regulations, the Court stated "[t]he FDA's statement is dispositive on the question of

> implicit intent to pre-empt *unless* either the agency's position is *inconsistent* with clearly expressed congressional intent, or subsequent developments reveal a change in that position." *Hillsborough County*, 471 U.S. at 714 (emphasis added).
>
> FN5. In *Bates*, the Supreme Court rejected the Environmental Protection Agency's position supporting preemption, explaining that the agency's argument in favor of preemption was "particularly dubious given that just five years ago the United States advocated the interpretation [i.e., no preemption] that we adopt today."544 U.S. at 449.

Here, the FDA's interpretation of regulations in 2006 (as expressed in the Preamble to the Final Rule) is in stark contrast to the FDA's position regarding the same regulations outlined in the FDA's 2000 Proposed Rules. As discussed previously, in the Preamble to Final Rule, which represents the finalized version of a proposal that was originally published in December 2000, the FDA fields comments submitted in response to the original proposal. In particular, the FDA addresses a number of comments expressing concern that the new labeling requirements "might have product liability implications" and requesting that the FDA "state in the final rule that FDA approval of labeling ... preempts conflicting and contrary State law, regulations, or decisions of a court of law...."71 Fed.Reg. at 3933-34. In responding to those comments, the Final Rule discusses why, in its view, FDA regulations preempt State law tort claims.

The position of the FDA as outlined in the Final Rule is opposite to the position of the FDA as stated in its December 2000 proposal of the same amendments (the "2000 Proposal.") *See*65 Fed.Reg. 81082 (Dec. 22, 2000). The 2000 Proposal explicitly stated that its regulations *donot* have preemptive effect. *Seeid.*Rather, the preamble to the 2000 Proposal explained that the FDA did not want its regulations to preempt state tort law, stating that "there should be little, if any, impact from this rule, if finalized, on the States" and that the "FDA has determined that this proposed rule *doesnot* contain policies that have federalism implications or that *preemptStatelaw."Id.*[FN6] (emphasis added).

> FN6. The Court notes too that the position taken by the FDA in the 2000 Proposal was entirely consistent with the position the Agency took in 1998 in the Preamble to the new regulations regarding consumer medications guides. *See*63 Fed.Reg. 66378 (Dec. 1, 1998.)Specifically, the comments stated that:
>
> > FDA's regulations establish the minimum standards necessary, but were not intended to preclude the states from imposing additional labeling requirements. States may authorize additional labeling....
> >
> > *Id.*

Also contained in the 2000 Proposal is a discussion of "Executive Order 13132: Federalism." *Id.* at 81103.In the 2000 Proposal, the FDA states that it has "analyzed this proposed rule in accordance with Executive Order 13132: Federalism ... [which] requires Federal agencies to carefully examine

actions to determine if they contain policies that have federalism implications or that preempt State law" and concluded that:

Because enforcement of these labeling provisions is a Federal responsibility, there should be little, if any, impact from this rule, if finalized, on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of Government. In addition, *this proposed rule does not preempt State law.*Accordingly, FDA has determined that this proposed rule does not contain policies that have federalism implications or that preempt State law.

Id. (emphasis added). However, in the Preamble to the Final Rule in 2006, the FDA has changed its position on the preemptive effect of the very same regulations while still maintaining that the FDA complied with Executive Order 13132:
[The FDA has] analyzed this final rule in accordance with the principles set forth in Executive Order 13132[and][h]ere, FDA has determined that the exercise of State authority conflicts with the exercise of Federal authority under the act.

In conclusion, the agency believes that it has complied with all of the applicable requirements under Executive Order 13132 and has determined that this final rule is consistent with the Executive order.

71 Fed.Reg. at 3967-68.

Because of the unexplained change in position, under the rule in *Bates* and *Hillsborough,* this Court must give less deference to the FDA's interpretation of its regulations.

Further, the 2006 Preamble was a novation, not subjected to prior public notice or comment while inverting the agency philosophy standing behind the regulations when proposed in 2000. While an agency's explanatory statement, composed after receiving comment upon the duly-published proposed regulations, is admittedly not itself subject to notice and comment before final publication, the abrupt rejection of the agency's own prior interpretation (while the regulations themselves are unchanged) suggests a degree of informality yielding an interpretation unhinged from the text and original intent of the regulations themselves.

(ii) The case law cited by Pfizer does not support its position that the FDA's interpretation should be given deference

Finally, as noted in the December 29 Opinion, the case law cited by Pfizer does not support its argument that the FDA's most recent opinion on preemption (i.e., the Preamble) is entitled to deference. Specifically, Pfizer cites *Medtronic, Inc. v. Lohr,* in which the Supreme Court held, in the context of medical devices, that the FDA "is uniquely qualified to determine whether a particular form of state law

'stands as an obstacle to the ... execution of the full purpose of objective of Congress,' and therefore, whether it should be pre-empted."518 U.S. at 496 (quoting *Hines,* 312 U.S. at 67);*seealsoHorn,* 376 F 3d at 171 (holding that, while the FDA's interpretation of statutes it has been charged by Congress with enforcing is not fully dispositive of the issues in the case, "the Supreme Court has instructed us that the FDA's preemption determinations are significant and should inform our interpretation" of the preemption clause of the Medical Device Amendments to the FDCA.)

As noted in the December 29 Opinion, "the issue before this Court is not one of express preemption, as presented in those cases [i.e., *Medtronic* and *Horn*] addressing the language set forth explicitly by Congress in the Medical Device Amendments ("MDA") of 1976 to the FDCA."*McNellis,* 2005 U.S. Dist. at *30. In *Medtronic,* the Supreme Court afforded deference to the FDA's determination of the preemptive effect of the medical device labeling regulations because it found that Congress had included an express preemption clause in the statute that explicitly authorized the FDA to preempt state law.*Medtronic,* 518 U.S. at 496. Congress, however, "did not extend such preemptive force to the regulation of pharmaceutical drugs in the FDCA."*McNellis,* 2005 U.S. Dist. at *30.

Thus, the reasoning in *McNellis* remains sound and this Court will not vacate its December 29 Order. The Preamble, without more, does not signal to this Court

Congressional intent to obviate state law. The issuance of the Preamble does not change the fact that Congress has not expressed an intent to preempt state failure-to-warn laws with respect to pharmaceutical drugs. *Seee.g.,Bates*, 544 U.S. at 449 ("If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly.") Thus, this Court remains "unwilling to find, as Pfizer would have it, that Congress intended to obviate the very state laws that provide remedies to consumers harmed by dangerous products and deceptive marketing in the absence of clear and compelling Congressional statement."*McNellis*, 2005 U.S. Dist. at *31.

3. The Recent Decision in *Colacicco v. Apotex, Inc.* does not Warrant Vacation of this Court's December 29 Order

In its supplemental submissions to this Court and at oral argument, Pfizer urges this Court to follow the recent decision of *Colacicco v. Apotex, Inc.*, 432 F.Supp.2d 514 (2006) in which a district court in the Eastern District of Pennsylvania granted summary judgment in favor of a defendant-pharmaceutical company on grounds that the FDA's regulations preempt state failure-to-warn laws. Specifically, in *Colacicco*, the district court gave substantial deference to the FDA's interpretation of its own regulations-as outlined in the Preamble-including the FDA's interpretation that Section 314.70 preempts state tort law. *Seeid.*

Having considered the holding in *Colacicco*, this Court will not depart from its holding that the Preamble should not be afforded the force of law. First, it is fundamental, but bears repeating, that *Colacicco* is not binding on this Court. Thus, while the *Colacicco* opinion is persuasive authority on this Court, the holding is not controlling. Second, for the reasons discussed *supra*, this Court respectfully disagrees with *Colacicco* that the "principles of deference do not allow [the Court] to question the FDA's interpretation of its own regulations ..." or that the Court must defer to the FDA's interpretation of its own regulations. *Id.* at 528.This overstates the deference due to an agency's interpretation under the present circumstances. Under well-settled precedent, where Congress has given no implicit empowerment to the FDA to preempt state law when the FDA deems it appropriate, this Court can not conclude that a high degree of deference is warranted where (1) the agency's interpretation has been inconsistent and (2) where there is no ambiguity in the federal regulations in question here. As such, the Court concludes that the recent decision in *Colacicco* does not warrant vacation of this Court's December 29 Order.

B. *Pfizer's Motion for Interlocutory Appeal*

As an alternative to vacating this Court's December 29 Order, Pfizer advocates that the Court certify the Order for immediate interlocutory appeal. Under 28 U.S.C. § 1292(b), interlocutory review is appropriate if the appeal (1) involves a controlling question of law;

(2) there is a "substantial ground for difference of opinion" about that question of law; (3) and where immediate appeal may materially advance the ultimate termination of the litigation.[FN7] *SeeKatz v. Carte Blanche Corp.*, 496 F.2d 747, 754 (3d Cir.1974). Interlocutory appeal under § 1292(b), however, is to be "used sparingly" and only in "exceptional" cases. *Hulmes v. Honda Motor Co.*, 936 F.Supp. 195, 208 (D.N.J.1996) (citing 16 Charles A. Wright, et al., *Federal Practice and Procedure*, § 3929 at 132 (1977)); *seeGardner v. Westinghouse Broadcasting Co.*, 437 U.S. 478, 480, 98 S.Ct. 2451, 57 L.Ed.2d 364 (1977). As such, even if Pfizer meets all three requirements, this Court may still deny certification as the decision to deny certification is entirely within the Court's discretion. *SeeBachowski v. Usery*, 545 F.2d 363 (3d Cir.1976). According to Pfizer, the preemption issue presented satisfies all three prongs of the interlocutory appeal test, while Plaintiffs oppose interlocutory appeal.

FN7.Section 1292(b) ("Interlocutory decisions") states, in pertinent part:

> When a district judge, in making in a civil action an order not otherwise appealable under this section, shall be of the opinion that such order involves a controlling question of law as to which there is substantial ground for difference of opinion and that an immediate appeal from the order may materially advance the ultimate termination of the litigation, he shall so state in writing in such order. The Court of Appeals which would have jurisdiction of an appeal of such action may thereupon, in its discretion, permit an appeal to be taken from such order, if application is

> made to it within ten days after the entry of the order....
>
> 28 U.S.C. § 1292(b).

1. Controlling Question of Law

The Third Circuit Court of Appeals has held that a "controlling question of law" is one in which, either: (1) if decided erroneously, would lead to reversal on appeal; or (2) is "serious to the conduct of the litigation either practically or legally."*SeeKatz*, 496 F.2d at 755 (citations omitted); *seePublic Interest Research Group of N.J., Inc. v. Hercules, Inc.*, 830 F.Supp. 1549, 1554 (D.N.J.1993). The Third Circuit has held that the preemptive scope of federal law is a "controlling question of law" for interlocutory appeal purposes. *SeeCipollone v. Liggett Group, Inc.*, 789 F.2d 181, 183 (3d Cir.1986) (finding that question of whether Federal Cigarette Labeling and Advertising Act preempts state common law claims granted review under Section 1292(b)); *seealsoC.E.R.1988, Inc. v. Aetna Casualty and Surety Co.*, 386 F.3d 263 (3d Cir.2004) (accepting for interlocutory appeal the question whether National Flood Insurance Program preempted state tort claims).

Here, there is little question that the preemption issue would be dispositive if decided in Pfizer's favor and therefore is "controlling" under either definition advanced by the Third Circuit in *Katz*.In addition, Plaintiffs concede that the summary judgment decision is a controlling question of law. (Pl.'s Opp.

Br. at 15.) As such, this Court finds Pfizer has satisfied the first requirement of the three-prong test.

2. Substantial grounds for a difference of opinion

The second requirement for an interlocutory appeal is that the question of law at issue present "substantial grounds for a difference of opinion."28 U.S.C. § 1292(b). Here, there is sufficient grounds for a difference of opinion for two reasons.

First, numerous conflicting decisions can constitute a sufficient basis for the finding that substantial differences of opinion exist. *SeeWhite v. Nix*, 43 F.3d 374, 378 (8th Cir.1994) (conflicting and contradictory opinions provide substantial grounds for a difference of opinion); *seealsoOyster v. Johns-Manville Corp.*, 568 F.Supp. 83, 88 (E.D.Pa.1983) (identification of "a sufficient number of conflicting and contradictory opinions" would provide substantial ground for disagreement). Here, the district courts throughout the country have come to different conclusions when addressing the same issue of law addressed by this Court in its December 29 Opinion. Specifically, the cases of *Colacicco,Dusek v. Pfizer, Inc.* and *Needleman v. Pfizer, Inc.* have held that state failure-to-warn claims were preempted by the FDCA and the FDA regulations. *SeeColacicco*, 432 F.Supp.2d at 536;*Dusek v. Pfizer, Inc.*, No. 02-3559, 2004 U.S. Dist. LEXIS 28056 (S.D.Tex. Feb. 20, 2004) and *Needleman v. Pfizer, Inc.*, No. 03-3074, 2004 U.S. Dist. LEXIS 15495 (N.D.Tex. Aug. 6, 2004). In contrast, a number of recent decisions addressing the same issue have

held, consistent with this Court's December 29 Opinion, that the FDA regulations establish minimum requirements such that they do not preempt state laws. *SeeJackson v. Pfizer, Inc.*, 432 F.Supp.2d 964 (2006); *Madden v. Wyeth*, No. 03-0167, 2005 U.S. Dist. LEXIS 19989 (N.D.Tex.2005); *Witczak v. Pfizer*, 377 F.Supp.2d 726 (D.Minn.2005); *Sybinski v. Pfizer*, No. YC047439 (Cal.Super. Ct., County of Los Angeles, July 12, 2005); *Zikis v. Pfizer*, No. 04-8104, 2005 U.S. Dist. LEXIS 27253 (N.D.Ill. Nov. 8, 2005); *Miles v. Pfizer*, 03-731C (M.D.La. Mar. 30, 2005); and *Cartwright v. Pfizer, Inc.*, 369 F.Supp.2d 876 (E.D.Tex.2005). Such a split in authority certainly constitutes a "sufficient number of conflicting and contradictory opinions."

Second, this Court can rest its conclusion that a substantial difference of opinion exists on the fact that the FDA's position-as established in the Preamble to the Final Rule-that Section 314.70 requires a finding of preemption, is in contrast to this Court's conclusions in its December 29 Opinion and today. Thus, Pfizer has satisfied the second prong of the analysis.

3. Resolution of Issues Will Materially Advance the Termination of Litigation

Third, Pfizer must prove that resolution of the issue to be appealed will materially advance the termination of the litigation. *See*28 U.S.C. 1292(b). This presents a closer issue. One "critical requirement [is] that [an interlocutory appeal] have the potential

for substantially accelerating the disposition of the litigation."*In re Duplan Corp.*, 591 F.2d 139, 148 n. 11 (2d Cir.1988). According to Pfizer, because none of Plaintiffs' claims can survive the dismissal of their failure-to-warn claim, the resolution of this issue may terminate this litigation at the summary judgment stage. Plaintiffs disagree. According to Plaintiffs, any grant of interlocutory review would have the opposite effect as it would halt this litigation as the Third Circuit reviewed the issue.[FN8]

> FN8. Plaintiffs also contend that, "because the Court's finding is so clearly supported by case law ... the Third Circuit would in all likelihood affirm the District Court's finding and trial would proceed as intended originally."(Pl.'s Opp. Br. at 17.)

In the December 29 Opinion and Order, this Court provides a roadmap by which a limited period of discovery will be undertaken during which Plaintiffs may acquire essential information and provide an expert's report, to determine whether Pfizer had "knowledge of a heightened risk of suicidality, which should have resulted in enhanced labeling beyond the FDA-approved warning."*McNellis*, 2005 U.S. Dist. LEXIS 37505 at *33. Specifically, the Court stated:

If Plaintiffs can prove to the factfinder that Pfizer had, prior to January 2003, "reasonable evidence of an association of a serious hazard [suicidality] with a drug [Zoloft or the SSRI class generally,]"*see*21 C.F.R. § 201.57(e), then the enhanced warning sought by Plaintiffs herein would not be preempted by the FDCA.

Id. at *33.If Plaintiffs then have no evidence, then their case cannot withstand summary judgment and the case will be over soon. If Plaintiffs survive summary judgment, then they will have demonstrated a reasonable basis upon which Pfizer shall have enhanced its warning of suicidality consistent with the governing regulations, 21 C.F.R. § 314.70(c)(6)(iii) and 201.57(e), and there is no conflict between the FDCA and the New Jersey Product Liability Act, and hence no conflict preemption. It is tempting to let this case go forward to this phase of renewal of the Defendant's summary judgment motion to test whether Plaintiffs can meet this standard, consistent with the FDA's regulations.

On balance, however, given the dispositive nature of the preemption issue, immediate appellate review will prevent the needless expenditure of resources on further discovery and renewed summary judgment motion practice, in the event Defendant were to succeed on appeal.

III. *CONCLUSION*

For the reasons discussed above, Pfizer's motion to vacate this Court's December 29 Order will be denied. The Court finds that the FDCA does not preempt a plaintiff from claiming that an FDA-approved warning was inadequate under State law if the plaintiff is able to demonstrate that the manufacturer knew of "reasonable evidence of an association of a serious hazard with a drug" and thus had a duty to

supplement its warning under 21 C.F.R. § 201.57(c). While Pfizer has demonstrated that new evidence (in the form of the Preamble) exists, this Court is not persuaded that the Preamble should be given the force of law under the circumstances explained above, nor should it persuade this Court to vacate its December 29 Order. However, this case is appropriate for interlocutory review as the appeal meets all three criteria under 28 U.S.C. § 1292(b). As such, this Court will grant Pfizer's motion to certify the Order for immediate interlocutory appeal.[FN9] Finally, because this Court is certifying the Order for immediate interlocutory appeal, it is appropriate for this Court to stay the proceedings pending a determination by the Court of Appeals.

> FN9. The precise question to be certified for interlocutory appeal is stated:
>
> > Whether that the United States Food and Drug Administration's requirements for the form and content of the labeling for the prescription antidepressant Zoloft preempted New Jersey's failure-to-warn law, under the doctrine of conflict preemption, where the FDA's regulations at 21 C.F.R. 201.57(e) and 314.70(c)(6)(iii) permit a manufacturer to unilaterally enhance its warning when the manufacturer has reasonable evidence of an association of a serious hazard with a drug.

The accompanying Order is entered.

UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

No. 06-3107

JOSEPH C. COLACICCO,
INDIVIDUALLY AND AS EXECUTOR OF THE ESTATE OF LOIS ANN COLACICCO, DECEASED,
Appellant

v.

APOTEX, INC.; APOTEX CORP., A SUBSIDIARY OF APOTEX, INC.; SMITHKLINE BEECHAM, d/b/a GLAXO SMITHKLINE

No. 06-5148

BETH ANN MCNELLIS,
ON BEHALF OF THE ESTATE OF THEODORE DEANGELIS,

DECEASED AND IN HER OWN RIGHT

v.

PFIZER INC.; JOHN DOES 1-5; ABC DOE CORP.; DEF DOE CORP., GHI DOE CORP.

PFIZER INC.,
Appellant

SUR PETITION FOR REHEARING

Present: SCIRICA, Chief Judge, SLOVITER, BARRY, AMBRO, FUENTES, FISHER, JORDAN, Circuit Judges, and RESTANI*, Judge

The petition for rehearing filed by Appellant Joseph C. Colacicco in No. 06-3107 and Appellee Beth Ann McNellis in No. 06-5148 in the above-entitled case having been submitted to the judges who participated in the decision of this court and to all the other available circuit judges of the circuit in regular active service, and no judge who concurred in the decision having asked for rehearing, and a majority of the circuit judges of the circuit in regular active service not having voted for rehearing by the court en banc, the petition for rehearing is denied. Judge Ambro

and Judge Fisher would have granted the petition for rehearing en banc.

By the Court,

/s/ Dolores K. Sloviter
Circuit Judge

Dated: May 5, 2008

PAR/CH/cc: All counsel of record

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*Hon. Jane A. Restani, Chief Judge, United States Court of International Trade, sitting by designation, as to panel rehearing only.

U.S. CONST. art. VI, cl. 2

This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.

Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780, 793

Section 202. Nothing in the amendments made by this Act to the Federal Food, Drug, and Cosmetic Act shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such amendments and such provision of State law.

21 U.S.C. § 321. Definitions; generally

For the purposes of this chapter—

* * *

(n) If an article is alleged to be misbranded because the labeling or advertising is misleading, then in determining whether the labeling or advertising is misleading there shall be taken into account (among

other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.

* * *

21 U.S.C. § 331. Prohibited acts

The following acts and the causing thereof are prohibited:

(a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.

(b) The adulteration or misbranding of any food, drug, device, or cosmetic in interstate commerce.

(c) The receipt in interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise.

(d) The introduction or delivery for introduction into interstate commerce of any article in violation of section 344, 355, or 360bbb-3 of this title.

* * *

21 U.S.C. § 332. Injunction proceedings

(a) Jurisdiction of courts

The district courts of the United States and the United States courts of the Territories shall have jurisdiction, for cause shown[1] to restrain violations of section 331 of this title, except paragraphs (h), (i), and (j).

(b) Violation of injunction

In case of violation of an injunction or restraining order issued under this section, which also constitutes a violation of this chapter, trial shall be by the court, or, upon demand of the accused, by a jury.

21 U.S.C. § 333. Penalties

(a) Violation of section 331 of this title; second violation; intent to defraud or mislead

(1) Any person who violates a provision of section 331 of this title shall be imprisoned for not more than one year or fined not more than $1,000, or both.

(2) Notwithstanding the provisions of paragraph (1), if any person commits such a violation after a conviction of him under this section has become final, or commits such a violation with the intent to defraud or mislead, such person shall be imprisoned for not more than three years or fined not more than $10,000, or both.

* * *

[1] So in original. Probably should have a comma.

21 U.S.C. § 352. Misbranded drugs and devices

A drug or device shall be deemed to be misbranded—

(a) False or misleading label

If its labeling is false or misleading in any particular. Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 355 or under section 262(a) of Title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 355(a) of this title or in section 262(a) of Title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Infor-mation that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term "health care economic information" means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.

* * *

(f) Directions for use and warnings on label

Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users, except that where any requirement of clause (1) of this paragraph, as applied to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting such drug or device from such requirement. Required labeling for prescription devices intended for use in health care facilities or by a health care professional and required labeling for in vitro diagnostic devices intended for use by health care professionals or in blood establishments may be made available solely by electronic means, provided that the labeling complies with all applicable requirements of law, and that the manufacturer affords such users the opportunity to request the labeling in paper form, and after such request, promptly provides the requested information without additional cost.

* * *

21 C.F.R. § 201.80. Specific requirements on content and format of labeling for human prescription drug and biological products; older drugs not described in § 201.56(b)(1).

Each section heading listed in § 201.56(d), if not omitted under § 201.56(d)(3), shall contain the following information in the following order:

* * *

(e) *Warnings.* Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. A specific warning relating to a use not provided for under the "Indications and Usage" section of the labeling may be required by the Food and Drug Administration if the drug is commonly prescribed for a disease or condition, and there is lack of substantial evidence of effectiveness for that disease or condition, and such usage is associated with serious risk or hazard. Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these serious adverse reactions and, if known, the approxi-mate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective use of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

* * *

21 C.F.R. § 314.70. Supplements and other changes to an approved application.

* * *

(c) *Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (moderate changes).* (1) A supplement must be submitted for any change in the drug substance, drug product, production process, quality controls, equipment, or facilities that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. If the supplement provides for a labeling change under paragraph (c)(6)(iii) of this section, 12 copies of the final printed labeling must be included.

(2) These changes include, but are not limited to:

(i) A change in the container closure system that does not affect the quality of the drug product, except those described in paragraphs (b) and (d) of this section; and

(ii) Changes solely affecting a natural protein, a recombinant DNA-derived protein/polypeptide or a complex or conjugate of a drug substance with a monoclonal antibody, including:

(A) An increase or decrease in production scale during finishing steps that involves different equipment; and

(B) Replacement of equipment with that of a different design that does not affect the process methodology or process operating parameters.

(iii) Relaxation of an acceptance criterion or deletion of a test to comply with an official compendium that is consistent with FDA statutory and regulatory requirements.

(3) A supplement submitted under paragraph (c)(1) of this section is required to give a full explanation of the basis for the change and identify the date on which the change is to be made. The supplement must be labeled "Supplement—Changes Being Effected in 30 Days" or, if applicable under paragraph (c)(6) of this section, "Supplement—Changes Being Effected."

(4) Pending approval of the supplement by FDA, except as provided in paragraph (c)(6) of this section, distribution of the drug product made using the change may begin not less than 30 days after receipt of the supplement by FDA. The information listed in paragraphs (b)(3)(i) through (b)(3)(vii) of this section must be contained in the supplement.

(5) The applicant must not distribute the drug product made using the change if within 30 days following FDA's receipt of the supplement, FDA informs the applicant that either:

(i) The change requires approval prior to distribution of the drug product in accordance with paragraph (b) of this section; or

(ii) Any of the information required under paragraph (c)(4) of this section is missing; the applicant must not distribute the drug product made using the

change until the supplement has been amended to provide the missing information.

(6) The agency may designate a category of changes for the purpose of providing that, in the case of a change in such category, the holder of an approved application may commence distribution of the drug product involved upon receipt by the agency of a supplement for the change. These changes include, but are not limited to:

(i) Addition to a specification or changes in the methods or controls to provide increased assurance that the drug substance or drug product will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess;

(ii) A change in the size and/or shape of a container for a nonsterile drug product, except for solid dosage forms, without a change in the labeled amount of drug product or from one container closure system to another;

(iii) Changes in the labeling, except for changes to the information required in § 201.57(a) of this chapter (which must be made pursuant to paragraph (b)(2)(v)(C) of this section), to accomplish any of the following:

(A) To add or strengthen a contraindication, warning, precaution, or adverse reaction;

(B) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage;

(C) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product;

(D) To delete false, misleading, or unsupported indications for use or claims for effectiveness; or

(E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.

(7) If the agency disapproves the supplemental application, it may order the manufacturer to cease distribution of the drug product(s) made with the manufacturing change.

* * *